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RESEARCH ARTICLE

A New Approach to Ceramics Based on the Tissue Reaction: A Versatile Ceramic for Pharmaceutical, Dental and Ancient Artifacts Applications Using Machine Learning (ML) Modeling

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ABSTRACT

The field of bioceramics has emerged as a critical component in various medical and dental applications, with calcium phosphate (CaP) materials like tricalcium phosphate (TCP) gaining significant attention. CaP bioceramics are valued for their exceptional biocompatibility, osteoconductivity, and ability to promote new bone formation, making them invaluable in the optimization of dental implant integration and performance. This study explores a novel approach to developing versatile CaP-based ceramics that can find applications in the pharmaceutical, dental, and even ancient artifacts preservation domains, leveraging the power of machine learning (ML) modeling techniques. Tricalcium phosphate, a widely studied CaP ceramic, was the focus of this investigation, as it can be fabricated with varying degrees of crystallinity and porosity to tailor its biodegradation and bone regeneration properties. Through the use of a feedforward artificial neural network (FFANN), the researchers were able to predict the changes in dental ceramics, biocompatibility, and tissue reactions across a wide range of non-toxicity and bone growth parameters. The FFANN modeling approach provided valuable insights into the relationships between these key attributes, allowing for the optimization of CaP-based ceramics for specific clinical and preservation applications. The versatility of TCP extends beyond dental implants, with applications in periodontal regeneration, tooth root repair, and even direct pulp capping procedures. By manipulating the material's composition and microstructure, researchers and clinicians can tailor the performance of CaP bioceramics to meet the diverse needs of the healthcare and cultural heritage sectors. As the field of bioceramics continues to evolve, the integration of advanced ML modeling techniques, such as the FFANN approach employed in this study, promises to unlock new possibilities for the development of innovative, tissue-friendly ceramics that can revolutionize dentistry, pharmaceutical formulations, and the preservation of precious ancient artifacts.

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INTRODUCTION

Bioceramics, which encompass calcium phosphate (CaP) compounds, have become essential materials in dentistry, particularly for dental implant applications. Their distinctive properties, including biocompatibility, osteoconductivity, and the ability to stimulate new bone formation, render these bioceramics invaluable for dental practitioners aiming to enhance implant integration and performance [1-3]. Among the various CaP bioceramics, tricalcium phosphate (TCP) has attracted considerable interest due to its versatility and beneficial characteristics. TCP can be engineered with different levels of crystallinity and porosity, which enables the optimization of its biodegradation and bone regeneration properties to meet specific clinical requirements [4-6]. Beyond dental implants, the use of TCP and other CaP bioceramics is being investigated for a diverse array of dental applications, including periodontal regeneration, tooth root repair, and direct pulp capping procedures. Dental implants have transformed the field of dentistry by offering a reliable and durable solution for the replacement of missing teeth [7-9]. However, the success of these implants largely hinges on their integration with surrounding bone, a process referred to as osseointegration. CaP bioceramics, such as TCP, have demonstrated significant efficacy in facilitating osseointegration. When employed as a coating on dental implants, these materials enhance the implant's capacity to bond with adjacent bone tissue [8-11]. The osteoconductive properties of TCP promote the formation of new bone cells on the implant surface, thereby establishing a robust connection with the jawbone. Additionally, the resorbable nature of TCP allows it to be gradually substituted by new bone as the implant integrates with the surrounding tissue.

This gradual replacement ensures that the implant is not only firmly anchored but also seamlessly integrated into the patient's natural dentition. While the use of CaP bioceramics in dental implants has been a significant focus, these materials are also finding applications in a variety of other dental treatments [10-14]. In the field of periodontal regeneration, porous TCP scaffolds have shown promise in promoting the regrowth of lost or damaged periodontal tissues, including the alveolar bone, cementum, and periodontal ligament. By providing a favorable microenvironment for cell migration and proliferation, these scaffolds can enhance the body's natural healing and regenerative processes [11-13]. CaP bioceramics are also being explored for the repair and restoration of tooth roots. In cases of extensive root damage or loss, these materials can be used as a biocompatible and osteoconductive filler, helping to support the remaining tooth structure and facilitate the integration of any necessary restorative work. Furthermore, the unique properties of CaP bioceramics have led to their investigation as direct pulp capping materials. When a tooth's pulp is exposed, these materials can be applied directly to the affected area, promoting the formation of reparative dentin and preventing further damage to the pulp tissue [14-16]. The versatility of TCP as a CaP bioceramic lies in its ability to be tailored to specific clinical needs. By adjusting the material's composition and microstructure, researchers and clinicians can optimize its performance for a wide range of dental applications. The degree of crystallinity, for example, can be manipulated to control the material's biodegradation rate. More crystalline TCP formulations tend to be more stable and slower to resorb, while less crystalline versions degrade more rapidly, allowing for faster replacement by new bone tissue [17-19]. Porosity is another important factor in the design of TCP-based materials. Porous scaffolds, with interconnected pore networks, can enhance bone ingrowth and vascularization, improving the overall integration and regenerative capacity of the material. Dense TCP coatings on implant surfaces can improve the implant's ability to integrate with the surrounding bone [20-22]. A feedforward artificial neural network (FFANN) with a single hidden layer was utilized in this study. This network architecture was employed to investigate and predict the attributes of interest, including dental ceramics, biocompatibility, and tissue reactions, across a broader range of non-toxicity and bone growth parameters as network inputs. Furthermore, linear regression analysis was conducted to evaluate the error associated with the neural network predictions. The predictions generated by the ANN were reviewed and assessed as part of the reporting and estimation process.

BIOINERT BIOCERAMICS

Bioinert bioceramics, a distinct category within the broader field of bioceramics, have emerged as a critical component in various medical applications, particularly in the realm of orthopedic and dental implants, where their exceptional mechanical strength, wear resistance, and chemical stability have made them invaluable; at the forefront of bioinert bioceramics are materials such as alumina (Al_2O_3) and zirconia (ZrO_2), which offer distinct advantages, with alumina renowned for its high hardness and compressive strength, making it a popular choice for joint replacement implants like hip and knee prostheses, while zirconia has gained prominence in dental implants due to its improved fracture toughness and enhanced aesthetics, and in addition to their structural and mechanical advantages, bioinert bioceramics also offer the benefit of radiopacity, allowing for improved visualization during medical imaging procedures, though the inert nature of these materials also presents some drawbacks, as they do not actively promote the integration and bonding of the implant with the surrounding bone tissue, a challenge that has led researchers to explore various strategies to enhance the bone-implant interface, such as modifying the surface topography or incorporating bioactive coatings, and as the field of bioceramics continues to evolve, bioinert materials are likely to play an increasingly pivotal role in the advancement of implant technology, contributing to improved patient outcomes and quality of life.

Figure 1 shows a comparison of titanium and ceramic dental implants. Titanium implants have been the standard in dental implant technology for decades, offering strong and durable support for artificial teeth. However, in recent years, ceramic implants have emerged as a promising alternative. Ceramic implants, made from zirconium oxide, are known for their natural tooth-like appearance, making them a more aesthetically pleasing option, especially for front-facing teeth. Additionally, ceramic implants are biocompatible and corrosion-resistant. While titanium implants remain a reliable choice, the rise of ceramic implants offers dental patients increased flexibility in selecting an implant material that best suits their individual needs and preferences. Alumina-based ceramics, glass ceramics, and zirconia ceramics have emerged as prominent bioinert biomaterials, each offering unique properties and applications within the field of biomedical engineering, with alumina-based ceramics such as Al_2O_3 renowned for their exceptional hardness, compressive strength, and wear resistance, making them a popular choice for orthopedic and dental implants due to their inert nature and reduced risk of adverse reactions, while glass ceramics like bioactive glass and glass-ceramics have gained attention for their ability to mimic the natural composition of human bone and teeth, possessing the capacity to form a strong bond with surrounding bone tissue and promote osseointegration, and zirconia ceramics, with their exceptional fracture toughness and improved aesthetic properties, have become increasingly prominent in dental applications, particularly in the realm of dental implants and restorations due to their superior mechanical strength, biocompatibility, and natural tooth-like appearance, collectively contributing to the advancement of biomedical engineering and the

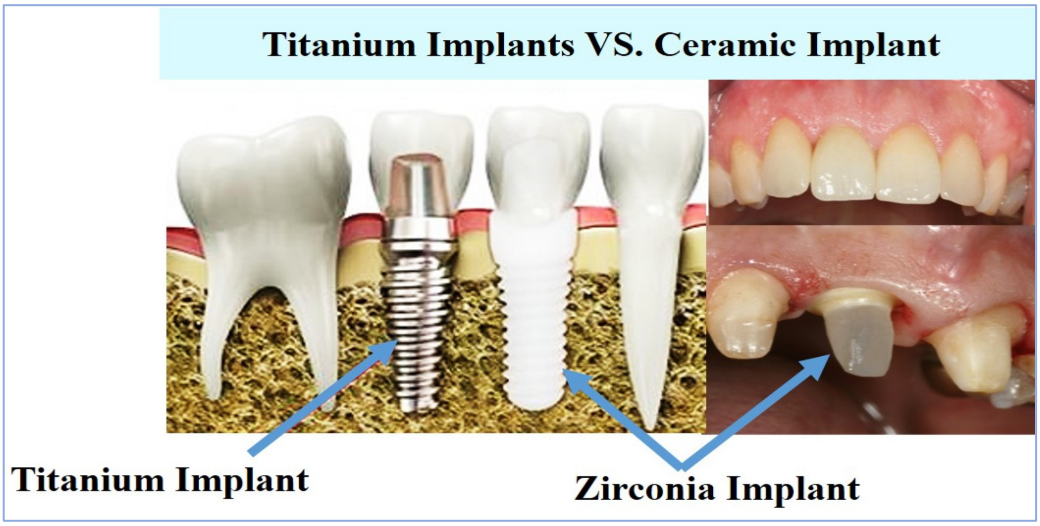

Fig. 1. Comparison of titanium and ceramic implants

restoration and replacement of damaged or missing tissues in the human body.

ACTIVE BIOCERAMICS

The field of active bioceramics has emerged as an exciting frontier in the medical industry, offering a range of innovative materials that go beyond the traditional bioinert ceramics, with bioactive glass ceramics such as Bioglass® and related compositions possessing the ability to form a strong bond with surrounding bone tissue and facilitate the integration of implants and prosthetic devices by releasing beneficial ions and promoting the growth of new bone, complemented by materials like wollastonite, a calcium silicate-based ceramic [1-3]. These ceramics that has demonstrated its potential in bone tissue engineering through its excellent biocompatibility and capacity to stimulate the formation of hydroxyapatite, the primary mineral component of bone, while the emergence of porous titanium alloy materials has leveraged the inherent strength and biocompatibility of titanium with a porous structure that mimics the architecture of natural bone [4-5]. Allowing for the ingrowth of new bone tissue and facilitating a stronger bond between the implant and the surrounding skeletal structure, collectively revolutionizing the medical industry and providing clinicians and researchers with a diverse array of materials that can be tailored to meet the specific needs of each patient, from enhancing implant integration to promoting bone regeneration, paving the way for improved patient outcomes and a brighter future in the field of biomedical engineering [6-9]. Non-absorbable bioceramics, also known as non-degradable bioceramics, have emerged as a prominent class of materials in the field of biomedical engineering, offering unique advantages and applications, with compositions typically based on materials such as Al_2O_3, ZrO_2, and silicon nitride (Si_3N_4), characterized by their exceptional hardness, wear resistance, and chemical stability, which make them highly suitable for long-term implantation within the human body, with their morphology ranging from dense, monolithic structures to porous frameworks that can facilitate the ingrowth of surrounding bone tissue, enhancing the integration and stability of the implant, and one of the key features of these non-absorbable bioceramics is their ability to form a direct connection with the surrounding bone tissue, a phenomenon known as osseointegration, allowing for the efficient transfer of load and leading to improved implant stability and long-term functionality, ensuring that these materials maintain their structural integrity and mechanical properties over extended periods, making them suitable for applications where long-term stability and durability are paramount, such as joint replacements, dental implants, and load-bearing orthopedic devices, leveraging the unique composition, morphology, and osseointegrative capabilities of non-absorbable bioceramics to develop advanced medical devices and implants that offer enhanced performance, improved patient outcomes, and a reduced risk of complications [10-13]. Bioglass, a pioneering and highly influential class of bioactive glass materials, has established itself as a key player in the field of biomedical engineering, characterized by its amorphous, non-crystalline structure that endows it with exceptional biocompatibility, bioactivity, and biodegradability, making it a highly desirable material for various medical applications, as the biocompatibility ensures safe integration into the human body, the bioactivity enables the formation of a strong bond with surrounding bone tissue, facilitating the integration of implants and prosthetic devices, and the controlled biodegradability allows for the gradual replacement of the material by the body's own regenerative processes, promoting tissue healing and regeneration, with the production of Bioglass typically involving the melting of a specific combination of raw materials, such as silicon dioxide (SiO_2), sodium oxide (Na_2O), calcium oxide (CaO), and phosphorus pentoxide (P_2O_5), to create a molten glass that can then be shaped and formed into various medical devices, coatings, or scaffolds, leading to the widespread adoption of Bioglass in a range of applications, including bone grafting, dental implants, and soft tissue repair, where its ability to stimulate the formation of new bone and integrate with the surrounding tissues have made it a valuable tool in the field of regenerative medicine. Absorbable or biodegradable ceramics have emerged as a promising class of materials in the biomedical engineering field, with Tricalcium Phosphate (TCP) being one of the most widely studied and utilized absorbable ceramic materials, characterized by its inherent biodegradability that allows it to slowly dissolve and be replaced by the body's own natural tissue as the healing and regeneration process takes place, a key advantage that enables the material to gradually resorb and create space for the natural tissue to grow and integrate, ultimately leading to the complete replacement of the implanted ceramic by the body's own structures, with the composition of TCP, consisting of calcium and phosphate ions, closely mimicking the mineral content of natural bone, enhancing its biocompatibility and facilitating the integration with the surrounding host tissue, while the released calcium and phosphate ions during the degradation process can also actively contribute to the stimulation of new bone formation, further promoting the regenerative process, setting absorbable ceramics like TCP apart from non-absorbable, or non-degradable, bioceramics and allowing for the seamless integration and remodeling of the implanted material, ultimately leading to improved long-term outcomes and the restoration of the body's natural structure and function.

Calcium phosphate

Calcium phosphate materials have emerged as a prominent class of biomaterials in the field of dentistry and bone regeneration, as they possess remarkable similarities to the mineral composition of natural teeth and bone, encompassing a diverse range of compounds like hydroxyapatite, tricalcium phosphate, and amorphous calcium phosphate, each exhibiting unique properties and characteristics that closely mimic the mineral phases found in the hard tissues of the human body, such as the enamel, dentin, and bone, with the growth-mediating properties of calcium phosphate materials making them invaluable in various dental and orthopedic applications, as they can actively participate in the mineralization and regeneration processes, promoting the formation of new bone and tooth structures, and facilitating the integration of implants with the surrounding natural tissues, while the bioactivity and resorbability of certain calcium phosphate phases, such as tricalcium phosphate, allow for the gradual replacement of the implanted material by the body's own regenerative processes, ensuring a seamless transition and the restoration of natural function, solidifying the versatility and biomimetic nature of calcium phosphate materials as key players in the field of dentistry and bone regeneration, offering promising solutions for a wide range of clinical challenges and paving the way for advancements in tissue engineering and regenerative medicine. Synthesis of HA from hydrothermal exchange of biological skeletal carbonate.

$$10CaCO_3+6(NH_4)_2+2H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2+6(NH_4)_2CO_3$$

Because HA is not the same as human apatite, its use has changed. The high temperature process causes high crystallization of HA and makes its absorption difficult during the bone regeneration process, which is the reason for this difference. Therefore, carbonate apatite is used as a substitute and a better candidate for bone replacement purposes compared to HA [14-18]. According to the results of various research studies, the biological activity of synthetic carbonate apatite is better than that of synthetic HA because the incorporation of carbonate into HA reduces crystallinity and increases solubility. Increased chemical reactivity and a change in crystal morphology resulted from weak bonding [19-23]. In this context, apatite carbonate will be more soluble in vivo than HA. The solubility of apatite carbonate increases the local concentration of calcium and phosphate ions, which are essential for new bone formation. In general, HA and fluorapatite (FA) ceramics are less soluble than TCP. But it is possible to absorb HA coatings on implants with time [24-28]. Table 1 shows that the calcium to phosphate (Ca/P) ratios for various calcium phosphate compounds commonly used in biomedical applications.

Table 1 serves as a valuable reference, highlighting the distinct compositions and characteristics of these materials. Tetracalcium phosphate (TTCP) has the highest Ca/P ratio of 2.0, while hydroxyapatite (HA) has a ratio of 1.67, closely mirroring the mineral composition of natural bone and tooth structure. Tricalcium phosphate (TCP), in its various crystalline forms (α', α, β, γ), exhibits a Ca/P ratio of 1.50, rendering it an attractive choice for bone regeneration and dental applications due to its biodegradable nature and ability to be gradually replaced by new bone tissue. Other calcium phosphate compounds, such as octacalcium phosphate (OCP), dicalcium phosphate dihydrate (DCPD), and calcium pyrophosphate (CPP), demonstrate varying Ca/P ratios, each with their unique properties and potential applications in the field of biomaterials and tissue engineering. This comprehensive table serves as a valuable resource for researchers and clinicians in selecting and tailoring the appropriate calcium phosphate material for specific dental and orthopedic treatments.

Table 1. Ca/P ratios for different calcium phosphates

Name	Abbreviation	Ca/P ratio
Tetracalcium phosphate	TTCP	2.0
Hydroxyapatite	HA	1.67
Tricalcium phosphate (α’, α ‘ β ‘γ)	TCP	1.50
Octacalcium phosphate	OCP	1.33
Dicalcium phosphate dihydrate (brushite)	DCPD	1.0
Dicalcium phosphate (montite)	DCP	1.0
Calcium pyrophosphate (α ‘ β ‘γ)	CPP	1.0
Calcium pyrophosphate dihydrate	CPPD	1.0
Heptacalcium phosphate	HCP	0.7
Tricalcium dihydrogen phosphate	TDHP	0.67
Calcium phosphate monohydrate	CPM	0.5

Tricalcium phosphate

Tricalcium phosphate, in both its alpha (α-TCP) and beta (β-TCP) crystalline forms, has become an increasingly important material in the field of dentistry due to its exceptional biocompatibility, osteoconductive properties, and ability to promote the regeneration of hard and soft oral tissues. In restorative dentistry, tricalcium phosphate is commonly incorporated into dental cements, composites, and sealers to enhance their bioactivity and facilitate the remineralization and repair of damaged tooth structures, such as caries, dental tubules, and other defects [29-33]. The gradual dissolution of tricalcium phosphate within these materials can stimulate the formation of hydroxyapatite, which is the primary mineral component of natural teeth, leading to improved integration with surrounding tooth tissues and enhanced long-term restoration success. Furthermore, tricalcium phosphate-based bone graft materials are widely utilized in periodontal and oral surgical procedures to fill bony defects and support the regeneration of alveolar bone and surrounding soft tissues, such as the gingiva [34-39]. The porous nature of tricalcium phosphate scaffolds allows for the ingrowth of new bone cells and blood vessels, facilitating the healing of periodontal tissues and improving the prognosis of treatments. Additionally, TCP has found applications in dental implantology, where it can be used to coat the surface of implants to improve osseointegration and enhance the structural and functional connection between the implant and the surrounding bone, leading to better implant stability and long-term success. The versatility of tricalcium phosphate in dental applications is further highlighted by its use in the development of advanced biomaterials, such as bioactive glasses and ceramics, which combine the unique properties of different calcium phosphate compounds to create innovative solutions for oral healthcare and rehabilitation.

Alpha tricalcium (α-TCP)

Alpha tricalcium phosphate (α-TCP) has become an important material in dental applications due to its biocompatibility, ability to promote bone regeneration, and potential to enhance the integration of dental materials with surrounding tooth structure and bone. In restorative dentistry, α-tricalcium phosphate (α-TCP) is utilized in dental cements and composites to enhance remineralization and facilitate the repair of damaged tooth structures. In periodontics, α-TCP-based bone graft materials are employed to address bony defects and promote the healing of periodontal tissues. Additionally, applying an α-TCP coating to dental implants can enhance osseointegration, resulting in improved implant stability and long-term success. The distinctive properties of α-TCP render it an essential material across multiple facets of contemporary dentistry, ranging from restorative treatments to implant and regenerative therapies.

Beta tricalcium(β-TCP)

Beta tricalcium phosphate (β-TCP) is another important calcium phosphate material that has found numerous applications in the field of dentistry. Similar to its alpha counterpart, β-TCP possesses excellent biocompatibility and osteoconductive properties, making it a suitable choice for a variety of dental treatments and procedures. In restorative dentistry, β-TCP is often incorporated into dental

Table 2. Properties of bioceramics in various field for using ANN modeling

Case	Input (%)		Output (%)		
	Non-Toxicity	Bone Growth	Dental Ceramics	Biocompatibility	Tissue Reactions
1	40%	30%	70%	20%	10%
2	60%	50%	80%	70%	60%)
3	45%	35%	65%	55%	75%
4	90%	80%	75%	65%	85%
5	35%	40%	75%	60%	65%

cements, composites, and sealers to enhance their bioactivity and promote the regeneration of damaged tooth structures. When used in these materials, the gradual dissolution of β-TCP can stimulate the formation of hydroxyapatite, which helps to remineralize and repair caries, dental tubules, and other defects in the tooth structure [42-46]. Furthermore, β-TCP-based bone graft materials are widely utilized in periodontal and oral surgical procedures to fill bony defects and support the regeneration of alveolar bone and surrounding soft tissues. The porous nature of β-TCP scaffolds allows for the ingrowth of new bone cells and blood vessels, facilitating the healing of periodontal tissues and improving the long-term prognosis of dental treatments. Additionally, β-TCP has found applications in dental implantology, where it can be used to coat the surface of implants to improve osseointegration and enhance the structural and functional connection between the implant and the surrounding bone [43-46]. The versatility of β-TCP in dental applications is further highlighted by its use in the development of advanced biomaterials, such as bioactive glasses and ceramics, which combine the unique properties of different calcium phosphate compounds to create innovative solutions for oral healthcare and rehabilitation.

ARTIFICIAL NEURAL NETWORKS (ANNS) MODELING

This study employed a feedforward artificial neural network (FFANN) to predict the changes in dental ceramics, biocompatibility, and tissue reactions across a wide range of 0-90% non-toxicity and bone growth parameters, using 5 experimental samples. The neural network architecture comprised input nodes for non-toxicity and bone growth, a hidden layer with 5 neurons (2 times the number of inputs plus one), and output nodes for dental ceramics, biocompatibility, and tissue reactions. A non-linear sigmoid activation function was utilized to capture the non-linear nature of the relationships and facilitate faster convergence of the network predictions. The error function was optimized using the gradient descent algorithm during the training and estimation stages.

To enhance the accuracy and convergence of the ANN, the input data from Table 2 was normalized prior to training, and the final results were denormalized to confirm they fell within the approved interval. The linear regression fit of the predicted results was compared to the y=x diagram of 100% accurate estimation based on the input targets from Table 2, to determine the error of the ANN. Additionally, the network's prediction accuracy was assessed through linear regression analysis of the normalized predicted results.

Figure 2 shows a schematic of the ANN architecture, consisting of a hidden layer with 5 neurons and 2 input nodes representing non-toxicity and bone growth, in order to predict the changes in dental ceramics, biocompatibility, and tissue reactions across 5 samples. The current study employed a feedforward artificial neural network (FFANN) to predict and optimize the performance of ceramic materials for various applications, including pharmaceutical, dental, and ancient artifacts preservation. Two key input variables were identified as critical factors: non-toxicity (%) and bone growth (%). Three output variables were chosen to evaluate the ceramic materials' performance: dental ceramics (%), biocompatibility (%), and tissue reactions (%). The FFANN model was developed using the selected input and output variables, comprising an input layer with two nodes, a hidden layer with five neurons, and an output layer with three nodes. A non-linear sigmoid activation function was employed, and the error function was optimized using the gradient descent algorithm. To enhance the accuracy and convergence of the FFANN model, the input data was normalized prior to training, and the final results were denormalized to ensure they fell within the approved interval.

RESULTS AND DISCUSSION

The field of bioceramics, particularly CaP materials like TCP, has become increasingly crucial in the realm of dentistry, especially for dental implant applications. CaP bioceramics are highly valued for their biocompatibility, osteoconductivity, and ability to promote new bone formation, making them invaluable tools for dental clinicians seeking to optimize implant integration and performance. The versatility of TCP, which can be fabricated with varying degrees of crystallinity and porosity to tailor its biodegradation and bone regeneration properties, extends beyond dental implants, with applications in periodontal regeneration, tooth root repair, and direct pulp capping procedures. The integration of CaP bioceramics, such as TCP, has been shown to enhance the osseointegration of dental implants by facilitating a strong and stable connection between the implant and the surrounding bone tissue. As research continues to refine the composition, microstructure, and processing of these materials, their role in modern dentistry is poised to expand, providing innovative solutions for a wide range of clinical challenges and paving the way for advancements in tissue engineering and regenerative medicine, further enhanced by the integration of machine learning modeling techniques like artificial neural networks to predict and optimize the performance of these versatile bioceramics. A feedforward neural network (FFANN) was developed according to Table 2 to predict the changes in dental ceramics, biocompatibility, and tissue reactions with increasing non-toxicity and bone growth. The indicative behaviors, including the changes in dental ceramics, biocompatibility, and tissue reactions within the range of 0-90% non-toxicity and 0-80% bone growth, were predicted and investigated. The neural network's predicted results for the changes in dental ceramics are shown in Figure 3 (a-b). The results indicate that as bone growth increases, dental ceramics growth increases, and from 40% onwards, the growth in dental ceramics stabilizes. However, with the increase in non-toxicity, the behavior of dental ceramics fluctuates, initially decreasing and then increasing.

Figure 4 (a-b) shows the neural network's predicted results for the changes in biocompatibility. The results show that as both non-toxicity and bone growth increase, biocompatibility increases, but this growth is observed after approximately 30% bone growth and 40% non-toxicity. These materials are favored due to their high biocompatibility, osteointegrative capabilities, and their similarity to the mineral components of natural bone. Additionally, bioceramics have great potential in the fabrication of porous and moldable ceramics, making them an excellent choice for use as scaffold materials in tissue engineering [38-40].

Advancements in technology have led to an

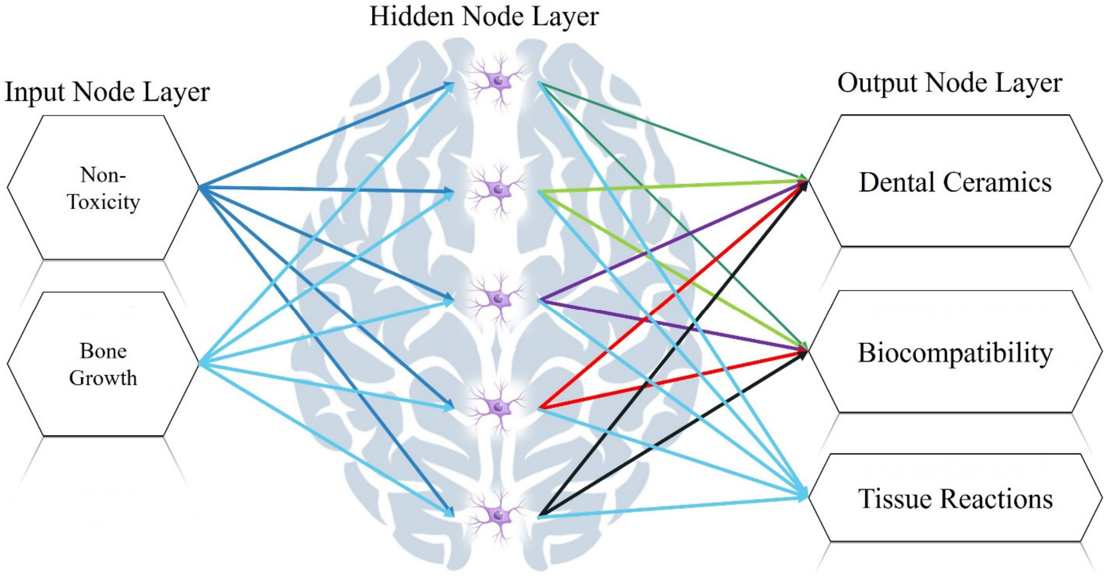

Fig. 2. Schematic of an ANN with a hidden layer, a new approach for predicting the tissue response of bioceramics based on TCP for dental materials applications

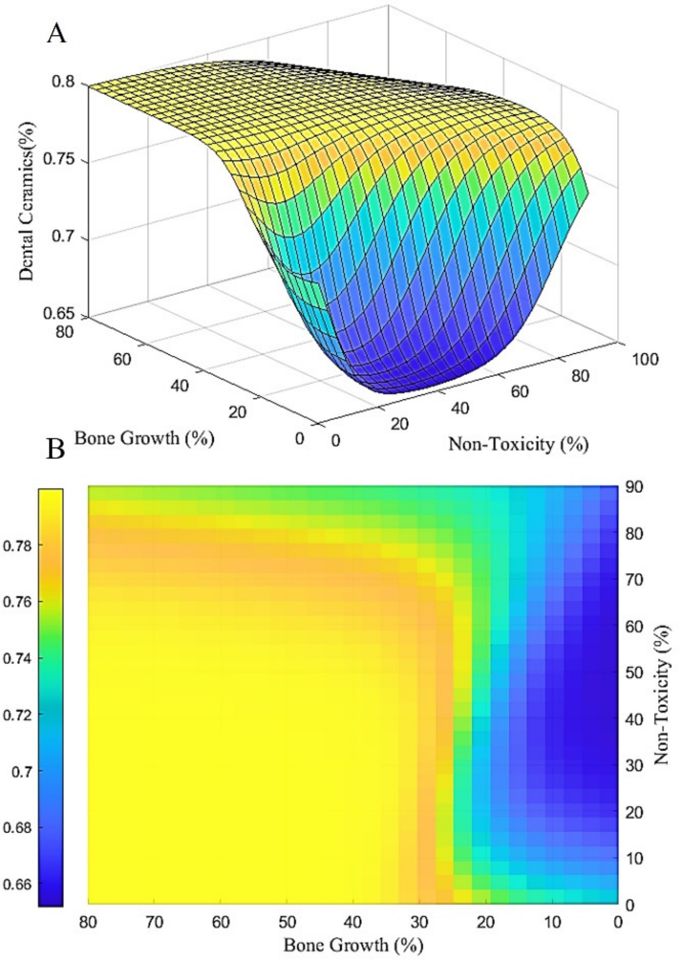

Fig. 3. Predictions made by the ANN to predict the performance of the dental ceramics tested a) front view and b) side view

increasingly diverse range of bioceramic shapes, functions, structures, and compositions, further expanding their potential applications in the field of regenerative medicine [38-40]. The neural network's predicted results for the changes in tissue reactions are shown in Figure 5 (a-b). The results indicate that as non-toxicity increases, tissue reactions increase, while an increase in bone growth leads to a decrease in tissue reactions.

The results obtained from the linear regression analysis based on the inputs and outputs are presented in Figure 6 (a-c). As expected, the ANN was able to accurately detect the targets in Table 2, with an error of less than 1%, showing its effectiveness in predicting dental ceramics, biocompatibility, and tissue reactions. Bioceramics are a specialized set of ceramics designed to restore and regenerate diseased or damaged parts of the human body [38-39]. Ceramics played a crucial role in the daily lives and cultural practices of ancient civilizations, serving both functional and artistic purposes that reflected their technological advancements and aesthetic values. Primarily utilitarian, ancient ceramics were used for cooking, storage, and serving food, with vessels varying in shape and size to meet specific needs, such as pots for boiling, jars for storage, and plates for serving. Beyond their practical applications, ceramics provided a canvas for artistic expression, adorned with intricate designs and motifs that showcased the creativity and cultural narratives of different societies. Many ceramic pieces also held symbolic meanings and were integral to rituals, such as funerary practices or religious

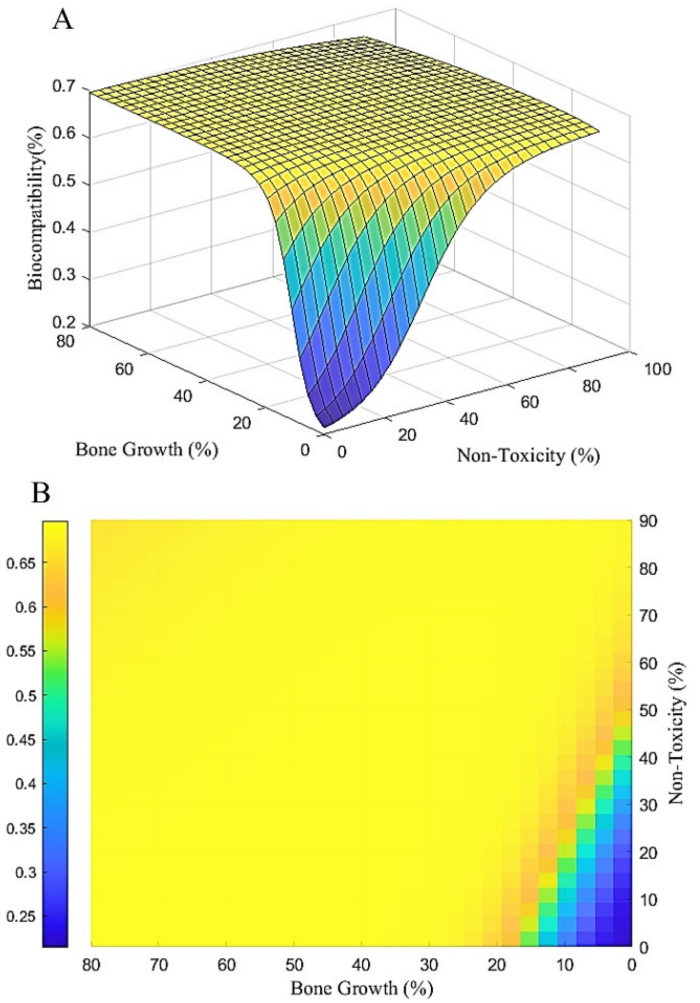

Fig. 4. Predictions made by the artificial neural network to predict the biocompatibility of the materials tested a) front view and b) side view

ceremonies, where they served as offerings or ritual vessels. The development of pottery techniques, including the potter's wheel and kiln construction, marked significant technological advancements that improved the quality and efficiency of ceramic production, facilitating trade through the mass production of standardized items. Additionally, ceramics often acted as historical records, preserving knowledge about language, mythology, and daily life through inscriptions and pictorial representations, thus contributing to our understanding of ancient cultures. The ceramics in ancient societies were essential for daily living, vessels of artistic expression, symbols of cultural identity, and records of historical knowledge, illuminating the complexities of past civilizations and their enduring legacies.

These materials have a high potential for use as scaffolding in tissue engineering applications. Traditionally, bioceramics have been employed to fill and repair defects in hard tissues, such as bone and teeth [30-33]. However, recent developments have also demonstrated promising applications of this class of biomaterials in the field of soft tissue engineering [30]. One particular type of bioceramic is beta-tricalcium phosphate (β-TCP) [35-38]. β-TCP is an ideal bone reparative agent, exhibiting excellent biocompatibility and osteogenic properties. It is utilized in the creation of bioceramic green parts by layering curable tricalcium

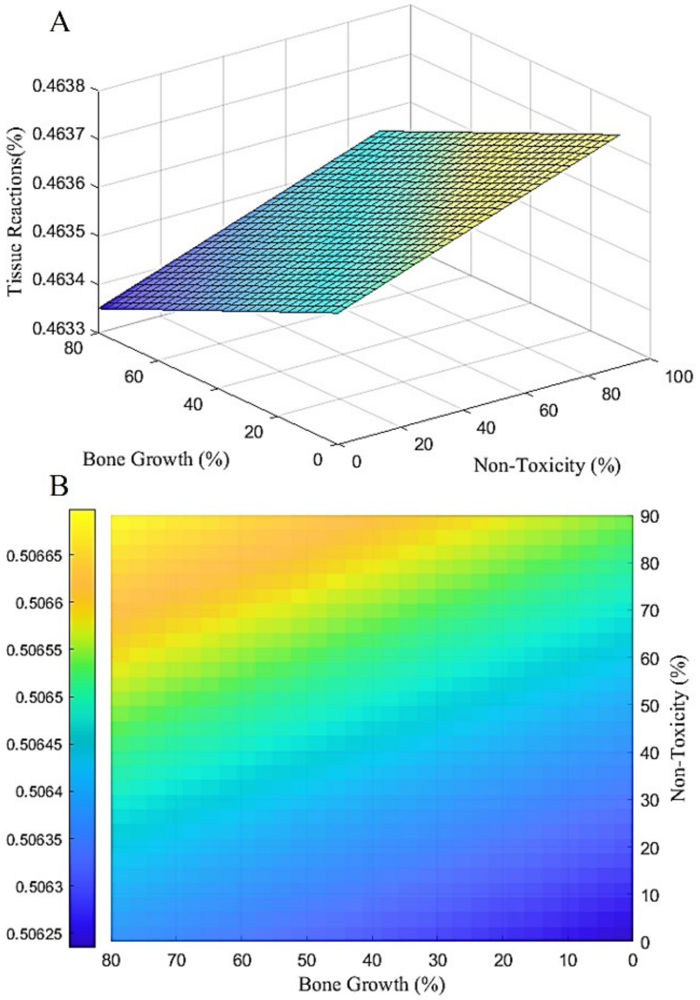

Fig. 5. Predictions made by the artificial neural network to predict the tissue reactions of the materials tested a) front view and b) side view

phosphate slurry with varying weight fractions of β-TCP [32-36]. In the field of dental materials, calcium phosphate-based bioceramics have gained significant traction in both orthopedic and dental applications [34-40]. One study investigates the significance of salivary C-reactive protein in both systemic and oral disorders, highlighting its potential as a biomarker for health assessments. Another explores the periodontal health of diabetic and non-diabetic adolescents, providing insights into the implications of diabetes on oral hygiene [41-46]. Additionally, research examines the interplay between rheumatoid arthritis and oral health, emphasizing the need for integrated medical approaches. Advances in biomaterials are notable, with discussions on innovative scaffold fabrication for bone regeneration, as well as novel nanoparticles for cancer hyperthermia applications [47-55]. The synthesis and characterization of new biomaterials underline the importance of material science in tissue engineering. Furthermore, the role of artificial intelligence in enhancing scientific analysis reflects the interdisciplinary nature of contemporary research. Ancient artifacts, especially ceramics, offer invaluable insights into the cultures, technologies, and daily lives of past civilizations, with applications spanning archaeology, anthropology, art history, and conservation. Ceramics reflect the social, economic, and spiritual aspects of societies, revealing trade relationships and cultural practices through their styles and decorations. They assist in chronological dating,

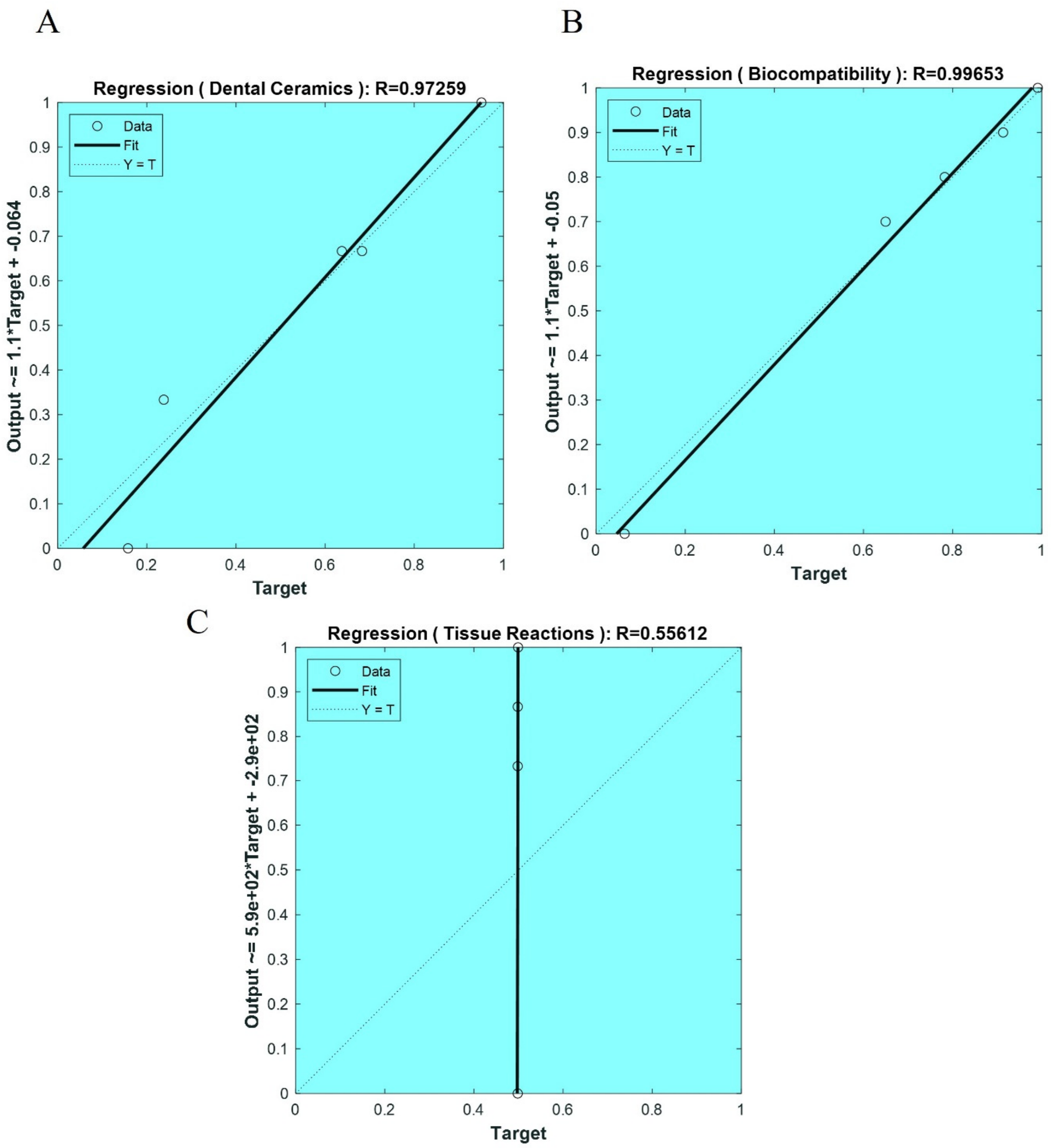

Fig. 6. Linear regression diagrams to assess the error of the ANN developed for predicting the performance of a) dental ceramics, b) biocompatibility, and c) tissue reactions.

as specific manufacturing techniques can be linked to particular time periods, while their distribution helps illustrate trade networks and cultural exchanges. Additionally, understanding ancient pottery techniques is crucial for conservation and restoration efforts. Functionally, ceramics served practical purposes such as cooking and storage, while also being a medium for artistic expression and ritual significance. The development of technologies like pottery wheels and kilns not only enhanced the quality of ceramics but also influenced trade dynamics. Moreover, ceramics often bear inscriptions that preserve knowledge about language, mythology, and historical events, making them essential for understanding the complexities of past societies and their interactions.

CONCLUSION

Providing non-toxicity and bone growth can lead to increased biocompatibility and tissue reactions of dental ceramics. Dental ceramics exhibit their optimal performance when bone growth is at its highest and non-toxicity is at its lowest. It can also be concluded that bone growth has a direct positive relationship with dental ceramics. Biocompatibility is maximized when both non-toxicity and bone growth parameters are at their peak levels. However, the effect of bone growth is more significant than non-toxicity in influencing biocompatibility. Both parameters have a direct positive relationship with biocompatibility. Tissue reactions are at their highest when non-toxicity is at its maximum and bone growth is at its minimum. This suggests that non-toxicity has a direct positive relationship with tissue reactions. The field of bioceramics has become increasingly integral to the advancement of modern dentistry, with calcium phosphate (CaP)-based materials such as hydroxyapatite (HA) and beta-tricalcium phosphate (β-TCP) emerging as the materials of choice due to their exceptional biocompatibility, tailored properties, and diverse applications; these CaP-based bioceramics closely mimic the natural composition of human bone and tooth enamel, allowing for seamless integration with surrounding tissues and minimizing the risk of adverse reactions, and their versatility extends beyond biocompatibility, with researchers developing advanced materials like HA/β-TCP composites that combine the beneficial properties of both components to create scaffolds and implants with superior mechanical performance and osteogenic potential, addressing the crucial need for effective subbone management in dental implantology through the use of CaP-based bioceramics that can serve as scaffolds supporting the in-growth of new bone tissue, while the incorporation of these bioceramics into the composition of dental materials such as cements, composites, and coatings has also led to enhanced mechanical properties and bioactivity, revolutionizing the way dentistry is practiced and paving the way for improved patient outcomes and a brighter, healthier smile. In conclusion, ceramics in ancient cultures were vital not only for practical uses such as cooking and storage but also as mediums for artistic expression and cultural identity. They served significant roles in rituals and technological advancements, while also preserving historical knowledge, thereby offering invaluable insights into the lives and beliefs of past civilizations.

AVAILABILITY OF DATA AND MATERIALS

The datasets supporting the conclusions of this study are included within the article.

COMPETING INTERESTS STATEMENT

The authors have declared that no competing interests exist.

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