

Systematic Review

Hydroxyapatite as bone graft materials to support dental implant treatment: systematic review

Fairuz Zahira Djaswandini¹
Andri Hardianto²
Abel Tasman Yuza²

¹Undergraduate study program,
Faculty of Dentistry, Universitas
Padjadjaran, Indonesia

²Department of Oral and
Maxillofacial Surgery, Faculty of
Dentistry, Universitas Padjadjaran,
Indonesia

* Correspondence:
andri.hardianto@fkq.unpad.ac.id

Received: 20 September 2024
Revised: 18 October 2024
Accepted: 20 November 2024
Published: 31 November 2024
DOI: [10.24198/pjd.vol36no3.55524](https://doi.org/10.24198/pjd.vol36no3.55524)

p-ISSN [1979-0201](#)
e-ISSN [2549-6212](#)

Citation:
Djaswandini FZ.; Hardianto A.;
Yuza AT.; Hydroxyapatite as bone
graft materials to support dental
implant treatment: systematic
review. Pad J Dent, November.
2024; 36(3): 415-426.

ABSTRACT

Introduction: Implant placement after tooth loss can prevent an alveolar bone resorption. Bone grafting is used to obtain adequate quantity and quality of alveolar bone to support dental implants. Hydroxyapatite is the primary synthetic bone graft biomaterial, with a composition and structure similar to natural bone. Hydroxyapatite biomaterials have been widely researched and developed. This study aims to summarize the modified HA materials that have been successfully used in supporting dental implant treatment. **Methods:** This review was conducted using a systematic review method that refers to systematic literature review simplification with PICO framework, based on PRISMA guidelines. Literature searches were performed through Science Direct, PubMed, Google Scholar, SAGE Journals, and Cochrane Library, for articles published between 2016 – 2021. Inclusion criteria for this review consisted of research articles on the use of hydroxyapatite bone graft in dental implant treatment. **Results:** Analysis was carried out on 11 articles on the use of hydroxyapatite bone graft in dental implant treatment with various material modifications: sintered, carbonated, eggshell-derived, 3D printed, obtained by sponge replica method, and in combination with rhBMP-2, PRF membrane, collagen membrane, and amniotic membrane. Additionally, hydroxyapatite also comes in several forms: porous block, granular, and nano-sized. Treatment success was observed through histology and histomorphometry analysis; SEM, XRD, FTIR, CBCT, and CT-Scan imaging; and ISQ value. **Conclusion:** This review demonstrates the modified hydroxyapatite, in combination with other materials or in various form, successfully supports dental implant treatment. This success is attributed to good osseointegration between bone and implant, bone growth, and increase in bone thickness, which are influences by the materials composition and morphology.

KEYWORDS

Bone graft, dental implant, Hydroxyapatite

INTRODUCTION

Tooth loss can occur due to extraction, periodontal disease, pulp disease, or trauma.^{1,2} Tooth loss leaves a void in the alveolar bone that is likely to resorb.¹ The Alveolar ridge can be resorbed by up to 50% within one year of tooth loss, with two-third of the resorption occurring in the first three months.³ One way to prevent bone resorption is by placing dental implants.⁴ Dental implants are becoming the treatment of choice to replace missing teeth given that they are aesthetically pleasing, comfortable, easy to clean, and able to preserve bone condition.¹

Dental implant placement site requires adequate alveolar ridge volume and quality.⁵ Rehabilitative measures are performed to obtain sufficient bone support

in quality and quantity to support dental implants.⁶ Alveolar ridge rehabilitation is conducted through bone grafting procedure. Natural bone will grow to replace bone graft materials and form new bones.⁷ The materials used to replace bone can be derived from the patient's own body, donor's body, artificial materials, synthetic materials, or natural materials.⁶

Hydroxyapatite (HA) $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ is a synthetic bone graft material that is commonly used to regenerate bone because of its similarity in composition and structure to natural bone.⁸ Its biocompatibility makes it the primary synthetic material of choice used for bone grafting, due to its ability to bind to natural bone without causing adverse effect to the body from toxic reactions or immune responses, leading to a promising treatment success.^{6,8-10}

Hydroxyapatite is the most widely researched biomaterials, and has been developed into various shapes and sizes, depending on the synthesis methods used.^{8,11} The size and shape of the material determine the mechanism of action and success of hydroxyapatite treatments in various biomedical applications.⁸ To date, many studies have been conducted using synthetic hydroxyapatite to enhance bone healing process, either being used alone in more beneficial form, by new production methods, or in combination with other materials.^{12,13}

With the continuous development of biomaterial technology, it's imperative to gather knowledge on the successful development of using hydroxyapatite as a bone graft material to support dental implant treatment, as there has been no previous studies that focuses on hydroxyapatite grafted implant treatment. The aim of this article is to summarize the modified hydroxyapatite materials successfully used to support dental implant treatments.

METHODS

This article uses the systematic review method, a form of knowledge synthesis that can efficiently produce information in a short and timely manner.¹⁴ Prior to the review, a PICO framework was used to develop research questions, as seen outlined in Table 1.

The articles were retrieved from Science Direct, PubMed, Google Scholar, SAGE Journals, and Cochrane Library databases. The writing process refers to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines. The search keywords used were "(Hydroxyapatite) AND (bone graft) AND (Dental implant)". The inclusion criteria for this research article include journals or research articles that specifically examine the use of hydroxyapatite as an effective bone graft materials for supporting dental implant treatment, with findings observed through clinical, analytical, and imaging analysis. The selected literature is indexed and ranked, written in English, and published between 2016 and 2021. Exclusion criteria include journals or research articles focus solely on animal testing of bone grafts publication later than 2016, articles without full-text access, those irrelevant to the topic, and duplicate entries.

During the initial search, 729 articles were identified, with 21 duplicates removed. Titles and abstracts of 708 articles were screened, resulting in the exclusion of 681 articles due to irrelevance. A total of 27 articles went through full-text assessment for eligibility, which led to the elimination of 16 articles. Ultimately, 11 articles met the eligibility and inclusion criteria. The PRISMA diagram illustrating the article selection process is presented in Chart 1.

Table 1. PICOS

Population	Tooth loss patients requiring bone augmentation prior to dental implant treatment
Intervention	Hydroxyapatite bone grafting
Comparative	-
Outcome	Osseointegration observed through implant stability after bone graft support

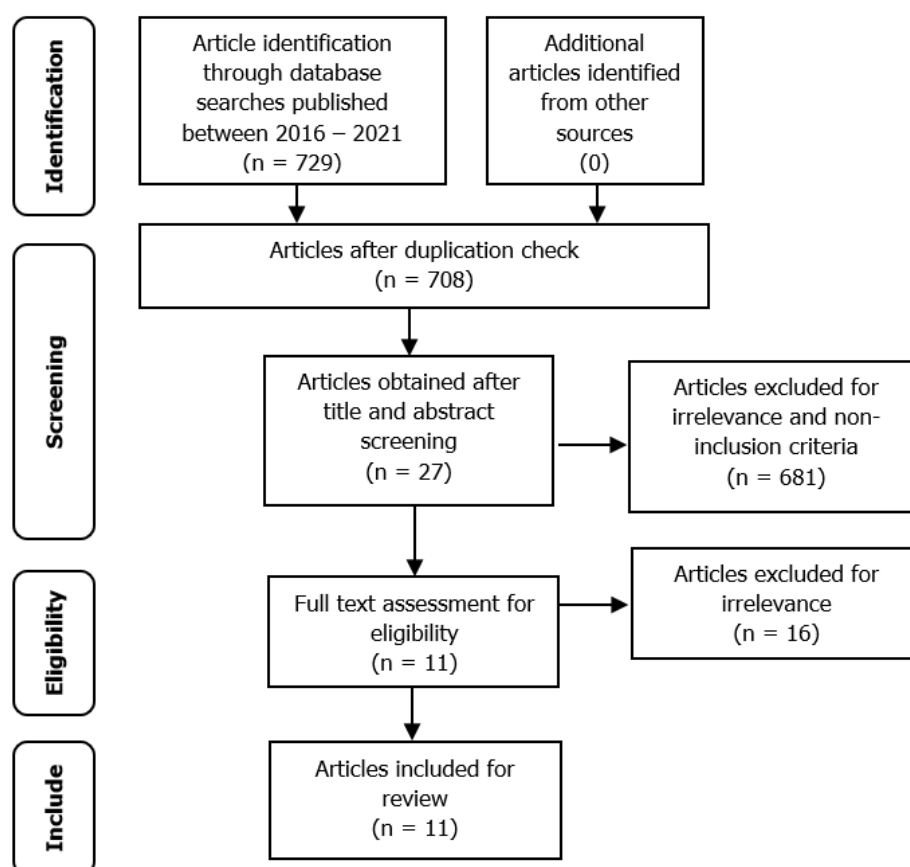


Chart 1. PRISMA diagram

RESULTS

We obtained 11 research articles that met the inclusion criteria. The modifications described in these articles included sintering process, eggshell-derived, 3D printing, carbonated hydroxyapatite (HA) produced through wet precipitation method, HA obtained via the sponge replica method, and combinations with rhBMP-2, PRF membrane, collagen membrane, and amniotic membrane. Additionally, various forms of HA were used; porous block, granular, and nano-sized. Data extraction from the eleven articles are summarized in table 2.

Table 2. Article Extraction Outcome

No	Articles	Participant	Materials	Procedure	Outcome
1	Application of Interconnected Porous Hydroxyapatite Ceramic Block for Onlay Block Bone Grafting in Implant Treatment: A Case Report Ohta, K., et al ¹⁶ . (2017)	- 1 subject - Aged 51 years - Requires implant treatment for extracted 21 tooth due to caries - Horizontal alveolar bone atrophy in the anterior region	Bone Graft: Interconnected porous hydroxyapatite ceramic (IP-CHA) block 6x7x3 mm Implant: Replace tapered groovy NP 3.5 x 10 mm	- Soft tissue opened with flap technique; an implant body installed into the alveolar bone - IP-CHA block placed over exposed implant thread - Soft tissue closed with an absorbable suture	6th month: - No complication, infection, abnormal pain, or hypoesthesia - ISQ value increased - IP-CHA block stable 16th month: - Stabilized IP-CHA block and implant 3rd year: - Good IP-CHA integration with host bone 5th year:

					- No problem with the implant and superstructure
2	<p>Histologic and Histomorphometric Comparison Between Sintered Nanohydroxyapatite and Inorganic Bovine Xenograft in Maxillary Sinus Grafting: A split-Mouth Randomized Controlled Clinical Trial</p> <p>Stacchi, C., et al¹⁷. (2017)</p>	<ul style="list-style-type: none"> - 28 subjects - Aged 39 – 79 years - Severe bilateral maxillary atrophy - Crestal height <3 mm - Needing MSFA 	<p>Bone graft: <u>Test group:</u> Granule sintered nanohydroxyapatite / NHA</p> <p><u>Control group:</u> Anorganic bovine bone / ABB (Bio-Oss)</p> <p>Membrane: Resorbable bovine collagen membrane</p> <p>Implant: BnxEvo implant</p>	<ul style="list-style-type: none"> - Soft tissue opened with full-thickness flap technique - MSFA with lateral approach - Bone graft materials inserted and covered with the membrane - The implants inserted 6 months after surgery - Healing abutment installed and metal-ceramic prosthesis screwed after 4 months - MSFA surgery with lateral approach - Bone graft material inserted through lateral window - Implant placement with full-thickness flap technique after 6 months - HA particles soaked into 1 mg/ml rhBMP-2 solution for activation to ensure hydration and flow through HA pores - Horizontal augmentation surgery with full-thickness mucoperiosteal flap technique 	<p>6th month:</p> <ul style="list-style-type: none"> - New bone formation and implants survival rate differences between NHA and ABB group are not statistically significant - Sufficient osseointegration between host bone and bone graft particles <p>12th month:</p> <ul style="list-style-type: none"> - All implants and prostheses function successfully - No biological or mechanical complication
3	<p>Histological and Micro-Computed Tomographic Observations After Maxillary Sinus Augmentation with Porous Hydroxyapatite Alloplast: A Clinical Case Series</p> <p>Nakata, H., et al¹⁸. (2016)</p>	<ul style="list-style-type: none"> - 3 subjects - Aged 64 – 73 years - Severe alveolar bone resorption due to periodontal disease or trauma - Clear maxillary sinus - Alveolar ridge to the sinus floor bone height 1-2 mm 	<p>Bone Graft: Porous Hydroxyapatite particles ϕ1-2 mm, 1 g</p> <p>Implant:</p> <ul style="list-style-type: none"> - Astra-tech implant system (ϕ3.75 x 10 mm) - Nobel-Replace Tapered (ϕ4.3 x 10 mm) 		<p>6th month:</p> <ul style="list-style-type: none"> - Stable implant torque during healing period - Mature bone cells and new blood vessel shows active bone remodeling and formation - Bone growth in the HA interspace observed with bone volume/tissue volume (BV/TV) \pm30% <p>Insertion:</p> <ul style="list-style-type: none"> - Insertion torque adequate to maintain implant stability (30 – 70 Ncm) <p>4-5th month:</p> <ul style="list-style-type: none"> - Statistically significant bone thickness increase within 4-5 months - Osseointegration observed around implant periphery
4	<p>Horizontal Ridge Augmentation of A Single Atrophic Site in the Anterior Maxilla Using Hydroxyapatite and rhBMP-2</p> <p>Maitre, G., et al¹⁹. (2020)</p>	<ul style="list-style-type: none"> - 13 subjects - Aged 19 – 28 years - Needed 1 tooth replacement - Residual bone width \leq 4 mm - Residual bone height \leq 2 mm 	<p>Bone graft:</p> <ul style="list-style-type: none"> - Osteo-conductor: Porous HA particles (80% porosity, d 3 mm) - Osteo-inductor: rhBMP-2 <p>Membrane: Fast resorbing microporous collagen membrane</p> <p>Implant: Conical implant 3.5 x 11 mm / 3.5 x 10 mm</p>		

5	Randomized Controlled Clinical Trial of Nanostructured Carbonated Hydroxyapatite for Alveolar Bone Repair	<ul style="list-style-type: none"> - 30 subjects - Aged 30 – 70 years - Indicated to undergo 1 dental extraction (for periodontal, trauma, or caries) - No soft tissue recesses - Adequate extraction site for the implant installation 	<p>Bone graft:</p> <ul style="list-style-type: none"> - Microspheres nanostructured carbonated hydroxyapatite (CHA) - BioOss® <p>Control group:</p> <ul style="list-style-type: none"> - Clot <p>Implant:</p> <ul style="list-style-type: none"> - Try-On® or Strong® implants 	<ul style="list-style-type: none"> - Bone graft materials inserted, stabilized with the membrane, and closed with absorbable sutures - Implant placed after 4 – 5 months - Healing cap placed after 3 months - CHA synthesized at 37°C, not sintered, prepared with wet precipitation method - Soft tissue opened with mucoperiosteal flap technique - Bone graft materials installed, and the wound closed with sutures - Implants installed after 90 days with mucoperiosteal flap procedure - Granular nHA synthesized from chicken eggshell waste for calcium precursors, using a rapid microwave processing technique - PRF membrane prepared by separating PRF component from centrifuged blood, and molded into thin sheet - nHA inserted immediately after tooth extraction, 	<ul style="list-style-type: none"> - Sufficient Adequate bone healing in all cases <p>Material analysis:</p> <ul style="list-style-type: none"> - Crystallinity of CHA are higher than BioOss <p>90th day:</p> <ul style="list-style-type: none"> - No complication or infection observed - CHA and BioOss clinically demonstrate the same bone density - New bone formation observed on CHA is higher than BioOss - Material remains are higher in BioOss <p>2nd week:</p> <ul style="list-style-type: none"> - Soft tissue healed with thick gingival biotype (>3 mm) - No graft material leaching <p>12th week:</p> <ul style="list-style-type: none"> - Increased bone density <p>24th week:</p> <ul style="list-style-type: none"> - Bone graft materials was clinically indistinguishable from neighboring bony tissue - Abundant bone formation (grade 3) in 56.52% sockets from
	Socket Preservation Using Eggshell-Derived Nanohydroxyapatite with Platelet-Rich Fibrin as A New Technique	<ul style="list-style-type: none"> - 11 subjects - Aged 15 – 45 years - Decayed teeth - Unrestorable teeth - Willing to undergo implant restoration 	<p>Bone graft:</p> <ul style="list-style-type: none"> - Granular nano hydroxyapatite (nHA) from chicken eggshell waste - 100 – 200 nm width and 0.5 – 1 μm long <p>Membrane:</p> <ul style="list-style-type: none"> - Platelet-Rich Fibrin (PRF) from autologous blood. <p>Implant:</p> <ul style="list-style-type: none"> - Nobel-Parallel conical connection root form 		

				covered with PRF membrane, and closed with sutures	histomorphometric analysis
7	<p>The Use of Three-Dimensional Printed Hydroxyapatite Granules in Alveolar Ridge Preservation</p> <p>Kijartom, P., et al²². (2017)</p>	<ul style="list-style-type: none"> - 5 subjects - Aged 33 – 45 years - Needed an anterior tooth extraction (endodontic failure, complicated crown-root fracture, and root caries) - Needed dental implant treatment 	<p>Bone graft:</p> <ul style="list-style-type: none"> - 3D printed hydroxyapatite granule 0,9 mm <p>Membrane:</p> <ul style="list-style-type: none"> - Collagen membrane 	<ul style="list-style-type: none"> - Implant installed after 24 weeks. - 3D printed granules transformed to HA through phosphorization reaction using disodium hydrogen phosphate - Granular HA inserted into extracted socket, layered with collagen membrane, and closed by crisscross sutures - Implants placed after 8 weeks. 	<p>Insertion:</p> <ul style="list-style-type: none"> - Insertion torque adequate to maintain implant stability (35 – 45 Ncm) <p>8th week:</p> <ul style="list-style-type: none"> - No complication, infection, or immune reaction - Good implant stability - New bone formation in and around grafting materials - Granular HA absorb and agglomerate blood more rapidly, making the structure sturdy and stable
8	<p>Application of Hydroxyapatite /Collagen Composite Material for Maxillary Sinus Floor Augmentation</p> <p>Ohba, S., et al²³. (2021)</p>	<ul style="list-style-type: none"> - Aged >20 years - Needing dental implant with MSFA for maxillary molar teeth 	<p>Bone graft:</p> <ul style="list-style-type: none"> - Hydroxyapatite/collagen (HAp/Col) composite - 80% HA, 20% collagen, 95% porosity <p>Implant:</p> <ul style="list-style-type: none"> - Osseo-Speed Finesia® Straumann® 	<ul style="list-style-type: none"> - MSFA surgery with lateral and crestal approach - HAp/Col immersed in patients' blood, then inserted to MSFA space - Implant placed into maxillary sinuses via lateral and crestal approach - Second surgery was performed after 3 months 	<p>3rd month:</p> <ul style="list-style-type: none"> - High implant survival rate (82.4%) - No adverse events occurred, the materials can be used safely - Higher bone height and thickness on the success group - Higher ISQ value on the success group
9	<p>Hydroxyapatite Block Produces by Sponge Replica Method: Mechanical, Clinical and Histologic</p>	<ul style="list-style-type: none"> - 13 subjects - Aged 41 – 64 years - Loss of maxillary premolar unilateral/bilateral or 	<p>Bone graft:</p> <ul style="list-style-type: none"> - Porous hydroxyapatite block obtained by the sponge replica method. <p>Implant:</p>	<ul style="list-style-type: none"> - HA block produced by impregnating polyurethane sponge block in the HA slurry, 	<p>Material analysis:</p> <ul style="list-style-type: none"> - The HA is well crystallized - The HA block has 85% porosity and a significantly

	Observations	fully/partially edentulous	Cylindrical implant	and the HA scaffold is sintered	high compressive strength
	Scarano, A., et al ²⁴ . (2019)	- Residual alveolar ridge height between 3 – 4 mm		- Access made with modified full-thickness triangular flap technique, and antrostomy performed	4th month:
				- Implant placed into alveolar bone socket, residual bone filled with HA blocks, and closed with a black polyamide suture.	- No inflammation, foreign body reaction, or pathological symptoms
				- Screw-healing abutment placed after 3-4 months	- New bone formation observed around and within HA block
				- MSFE with elevated full-thickness mucoperiosteal flap technique	
	Maxillary Sinus Floor Elevation Using Hydroxyapatite nano Particles VS Tenting Technique with Simultaneous Implant Placement: A Randomized Clinical Trial	- 19 subjects - Aged 24 – 59 years - Atrophic posterior edentulous maxillary ridge - Needing fixed prosthetic rehabilitation - Residual alveolar bone height 4 – 6 mm	Bone graft: - Nano hydroxyapatite (nano streams, Hydroxyapatite nanoparticles)	- Osteotomy with standard sequential implant protocol followed with implant insertion	Insertion: - No infection, dehiscence, or oroantral communication - All implant in both group stable
10	Khaled, H., et al ²⁵ . (2018)		Membrane: Resorbable collagen membrane	- HA nanoparticle mixed with sterile saline packed in a disposable syringe, then packed into grafted group (A)	6th month: - Higher bone density and height gain in grafted group
			Implant: Cleanant	- The window covered with membrane and sutured with an interrupted suture.	- Bone formation covered the whole implant in grafted group
				- PRF membrane prepared by separating PRF component from	- Higher ISQ value in grafted group
	Effect of nano-hydroxyapatite and platelet-rich fibrin covered by the amniotic membrane on	- 30 subjects - Mean age was 37.5 ± 2.3 years - Had edentulous space in the	Group I: nHA Group II: nHa + AM Group III: nHA + PRF + AM		Insertion: - ISQ value are higher in group II
11			Bone graft:		3rd month:

osseointegration after mandibular piezoelectric ridge splitting	posterior mandible	nHA, 19 nm	centrifuged blood, cut into small pieces, and mixed with nHA	- Higher bone density increases in group III
Altaweel, A.A., et al ¹³ . (2021)	- Alveolar ridge width 3 – 5 mm - Alveolar ridge height at least 8 mm	Membrane: Amniotic membrane 25 cm ²	- Soft tissue opened with full-thickness flap technique	6th month: - Higher bone width increases in group III - Higher bone density increases in group III
		Platelet-Rich Fibrin: PRF prepared with Dohan technique.	- Osteotomy performed, and 2 implants inserted in each site	12th month: - Stable osseointegration after 1 year - Higher bone density increases in group III - Higher marginal bone loss in group I
		Implant: Zimmer implants® 4.2 – 4.8 mm diameter, 8 – 12 mm long	- The gaps filled with graft materials according to the test group - Wound closed with interrupted non-resorbable sutures. - implant abutment placement after 6 months	

ISQ: Implant Stability Quotient; rhBMP-2: recombinant human bone morphogenetic protein-2; MSFA: Maxillary Sinus Floor Augmentation; PRF: Platelet-Rich Fibrin

DISCUSSION

Hydroxyapatite (HA) is the most widely used synthetic biomaterial in bone grafting because it has inorganic components and a crystal structure similar to natural bone, and it is the most stable calcium phosphate compound under physiological conditions, such as temperature, pH, and body fluids.⁸⁻¹⁰ Its use as a bone graft material has been continuously developed by modifying its shape and size or combining it with other materials to achieve the desired biological and mechanical properties. In the dental field, HA is widely used as a metal implant coating material to promote osseointegration between bone and implant in dental implant treatment. The success of bone grafting is determined by the formation of new bone, osseointegration between the bone and implant, and the stability of the dental implant.^{25,31}

The porous structure accelerates bone formation by facilitating a space for new bone and blood vessel growth, cell adhesion, and maintaining the bone volume stability.^{19,27} Block-shaped HA can be transported by clamping it with forceps, but its insertion can be challenging due to poor fitting. Ohta *et al.*¹⁶ used interconnected porous hydroxyapatite ceramic (IP-CHA) blocks for onlay bone grafting. IP-CHA can be pre-fabricated to match the shape and size of a patient's alveolar ridge.

In contrast to conventional porous CHA, which has limited interconnecting structure, IP-CHA has a fully interconnected pore structure. This structure exhibits biocompatible and osteoconductive properties, allowing bone growth around and within the pore, thereby promoting osseointegration.^{24,28} Imaging analysis demonstrate a subtle transition between the IP-CHA block and alveolar bone,

indicating good integration. The HA block used in the observation by Scarano et al.²⁴ was produced using the sponge replication method, which can also be customized in shape and size. This method involves impregnating polyurethane (PU) sponge in a HA and polyvinyl alcohol (PVA) slurry. The final HA framework was obtained by sintering at 1300°C for 3 hours, resulting in well crystallized HA. Heat treatments, such as sintering, enhance material crystallinity, thereby improving its mechanical strength and decreasing its dissolution rate.²⁰

Histological analysis revealed new bone growth both inside and outside the materials, along with marrow spaces and new blood vessels. Ohba et al.²³ used hydroxyapatite/collagen (HAp/Col) composite block consisting of 80% HA and 20% collagen, with a porosity of 95%. Materials containing collagen exhibit hemostatic properties, enabling material coagulation and stabilization. High porosity accelerates the formation of bone and blood vessel. Prior to use, HAp/Col was immersed in a patient's blood until it became elastic like a sponge. The elastic behavior facilitates the application of HAp/Col as it adapts easily to an intricate cavity.

In contrast with block-shaped HA, the granular form could adjust to the existing space, but sometimes the granule may scatter in the wound during insertion.²³ Nakata et al.¹⁸ used granular-shaped porous HA which quickly absorbed and integrated with blood, forming a firm and immobile structure.²² Histological and radiographic analysis showed the presence of a new bone and blood vessel-forming cells around and within the materials.

The ingrowth of porous materials increased the load-bearing ability compared to non-porous materials. Maitre et al.¹⁹ used porous granular HA, immersed in active ingredient *recombinant human bone morphogenetic protein-2* (rhBMP-2) solution. RhBMP-2 acts as an osteoinducer due to its ability to accelerate bone formation by promoting MSCs differentiation into osteoblast cells. CBCT analysis revealed a significant increase in average/mean bone thickness, which was further corroborated by a histologic analysis demonstrating adequate new bone growth to support implant insertion.

Kijartorn et al.²² produced 3D-printed granules using a 3-dimensional (3D) printing machine and converted it into HA through a phosphorization reaction. XRD and SEM analysis showed that the 3D-printed HA had low crystallinity, so it quickly absorbed and mixed with blood, agglomerating the material to become firm and immobile during the insertion process into the cavities.

Nano-sized HA developed to mimic natural bone composition, which showed enhanced biomechanical properties. Compared to a conventional form of HA, it exhibits improved biological performance, and the small nanoparticle size has a larger surface area, which results in a faster resorption rate.^{12,25,29} Stacchi et al.¹⁷ used sintered nano hydroxyapatite (nHA) in granular form. The nanosized material is easier to produce due to its lower sintering temperature.^{12,25,29}

Sintered nHA showed osteoconductive potential and good osseointegration, with new bone and blood vessel formation in the particles. Khaled et al.²⁵ used nHA mixed with sterile saline to get a soft consistency for insertion, then covered it with a collagen membrane to prevent intrusion of the implant body into the maxillary sinus. Collagen membranes had high biocompatibility and were bioactive, so they could promote tissue healing and modulate osteogenic processes.¹⁹ Altaweel et al.²⁶ used nHA in conjunction with Platelet Rich Fibrin (PRF) and covered by Amniotic Membrane (AM).

The use of PRF stimulates osteoblast proliferation and differentiation, facilitates angiogenesis, and enhances bone density.³³ The leukocyte in PRF played a role in regulating inflammation and infection. PRF has a hemostatic effect that maintains the stability of nHA graft particles.^{13,30} AM acted as a scaffold for cell proliferation and differentiation. AM accelerates the wound healing process by increasing epithelialization, and has anti-microbial and anti-viral properties.¹³ The

implant stability and bone density value in the test group using nHA in conjunction with PRF and AM were higher compared to the test group using HA alone.

Kattimani et al.²¹ synthesized nHA granules from calcium in chicken eggshells through a rapid microwave process. The use of eggshells as a source of synthesis is considered environmentally friendly and has no potential for disease transmission. This study used a PRF membrane to seal the grafting area and prevent leaching in the early implantation period. The eggshell-derived nHA indistinguishably merged into the neighboring bony tissue, and bone density increase was observed with no material leaching. Resende et al.²⁰ synthesized carbonated nHA through wet precipitation method without heat treatment, modified by substituting phosphate ions (PO_4^{3-}) in the B-type HA structure with carbonate ions (CO_3^{2-}). Non-sintered carbonated HA has lower crystallinity, therefore more biodegradable with a higher presence of neoformed bone.

The success of dental implant is influenced by primary stability. The insertion torque must be sufficient to hold the implant firmly in place, preventing micro-movements that may interfere with the osseointegration process. The insertion torque used in 3D-printed HA²² was 35 – 45 Ncm, and in porous HA with rhBMP-2¹⁹ was 30 – 70 Ncm. Insertion torque >50 Ncm can withstand implant micromovement without damaging the bone. However, an insertion torque of 20 – 25 Ncm, as used in porous HA¹⁸, can provide sufficient stability to prevent movement during the healing period.

This is consistent with Greenstein's³² statement that there is no definite minimum torque required to achieve primary stability. The implant stability quotient (ISQ) values in this study ranged from a low of 61.0 ± 13.3 (medium stability) to a high of 78 ± 5 (high stability). These ISQ values indicates good implant stability in alveolar bone augmented with HA bone graft. In clinical observation, there were no biological or mechanical complications reported; foreign body induced infection and inflammation; local and systemic immune reactions; pathological signs; dehiscence; or hypoesthesia throughout the study.^{16-18,20-26} The tissue seal remained intact, preventing material loss or leaching.

This article has limitations, including a narrow scope of discussion, the absence of a risk of bias assessment, and the involvement of only one researcher in analysis process. Further studies are necessary to explore the future clinical application of HA-based technologies.

CONCLUSION

Within the confines of the research studied thoroughly, HA reported a clinical success in supporting dental implant stably due to favorable osseointegration between bone and implant, as well as increased bone growth, thickness and density. Theoretical implications of this study suggest that the morphology and composition of HA materials influence their biological and mechanical properties, because its resemblance to natural bone promotes integration between the materials and the host, thus affecting the stability of implant embedded in the material. A smaller material may increase material resorption rate due to a larger surface area, which may induce surface reactivity. The material's porosity may promote osteoconductivity by providing a scaffold for cellular growth within and around the material. Additionally, material incorporation may enhance osteoinductivity and accelerate the healing period by facilitating cell growth necessary for new bone and blood vessel formation. The practical implication of this research is to provide dentists with considerations for selecting bone graft materials to rehabilitate alveolar bone defects.

Author Contributions: Conceptualization, H.A, D.F.Z, and Y.A.T.; methodology, H.A, D.F.Z, and Y.A.T.; validation, H.A dan Y.A.T.; formal analysis, H.A, D.F.Z, and Y.A.T.; investigation, D.F.Z; resources, H.A; data curation, H.A, and Y.A.T.; writing original draft preparation, H.A, D.F.Z, and Y.A.T.; writing review and editing, H.A, D.F.Z, and Y.A.T.; visualization, D.F.Z; supervision, H.A, and

Y.A.T.; project administration, D.F.Z.; funding acquisition, H.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: The data that support the findings of this research are available from the corresponding author, upon reasonable request

Conflicts of Interest: The authors declare no conflict of interest.

REFERENCES

1. Yamada M, Egusa H. Current bone substitutes for implant dentistry. *J Prosthodont Res* [Internet]. 2018. Apr; 62(2):152–161. <https://doi.org/10.1016/j.jpor.2017.08.010>
2. López-Gómez SA, González-López BS, Scougall-Vilchis RJ, Pontigo-Loyola AP, Márquez-Corona M de L, Villalobos-Rodelo JJ, et al. Tooth loss in patients with and without diabetes: A large-scale, cross-sectional study of Mexican adults. *J Am Dent Assoc* [Internet]. 2020;151(4):276–86. Available from: <https://doi.org/10.1016/j.adaj.2019.12.015>
3. de Oliveira GB, Rebello IMC, Montanha Andrade K, Araujo NS, dos Santos JN, Cury PR. Evaluation of alveolar process resorption after tooth extraction using the socket shield technique without immediate installation of implants: a randomised controlled clinical trial. *Br J Oral Maxillofac Surg*. 2021;6–11. Available from: <https://doi.org/10.1016/j.bjoms.2021.04.001>
4. Masaki C, Nakamoto T, Mukaibo T, Kondo Y, Hosokawa R. Strategies for alveolar ridge reconstruction and preservation for implant therapy. *J Prosthodont Res*. 2015;59(4):220–8. Available from: <https://doi.org/10.1016/j.jpor.2015.04.005>
5. Adhikari K, Tandukar A, Kumar B, Utilizing a Bioscaffold for Socket Preservation: A Case Report. *J Nepal ...* [Internet]. 2018. Jun; 1(1): 52–55. <https://doi.org/10.3126/jnprossoc.v1i1.23851>
6. Kumar R V, Udayshankar V, Prakash P, Jain V. Bone graft materials used in dental implants: A review. *IP Ann Prosthodont Restor Dent*. 2019;5(3):58–62. <http://doi.org/10.18231/j.aprd.2019.014>
7. Kumar P, Vinitha B, Fathima G. Bone grafts in dentistry. *J Pharm Bioallied Sci*. 2013;5(SUPPL.1):125–8. <https://doi.org/10.4103/0975-7406.113312>
8. Mazumder S, Nayak AK, Ara TJ, Hasnain MS. Hydroxyapatite composites for dentistry. *Applications of Nanocomposite Materials in Dentistry*. Sawston: Elsevier Inc.; 2019. 123–143 p. Available from: <https://doi.org/10.1016/B978-0-12-813742-0.00007-9>
9. Dewi AH, Ana ID. The use of hydroxyapatite bone substitute grafting for alveolar ridge preservation, sinus augmentation, and periodontal bone defect: A systematic review. *Heliyon*. 2018;4(10). Available from: <https://doi.org/10.1016/j.heliyon.2018.e00884>
10. Kattimani VS, Kondaka S, Lingamaneni KP. Hydroxyapatite—Past, Present, and Future in Bone Regeneration. *Bone Tissue Regen Insights*. 2016;7:9–19. <https://doi.org/10.4137/BTRI.S36138>
11. Varadavenkatesan T, Vinayagam R, Pai S, Kathirvel B, Pugazhendhi A, Selvaraj R. Synthesis, biological and environmental applications of hydroxyapatite and its composites with organic and inorganic coatings. *Prog Org Coatings*. 2021;151(September 2020):106056. Available from: <https://doi.org/10.1016/j.porgcoat.2020.106056>
12. Zhao R, Yang R, Cooper PR, Khurshid Z, Shavandi A, Ratnayake J. Bone grafts and substitutes in dentistry: A review of current trends and developments. *Molecules*. 2021;26(10):1–27. <https://doi.org/10.3390/molecules26103007>
13. Abdelqader Altaweel A, Aziz Baiomy Abdullah Baiomy A, Abdel-Hameed Elsayed S. Effect of Nano-hydroxyapatite and platelet-rich fibrin covered by the amniotic membrane on osseointegration after mandibular piezoelectric ridge splitting. *Saudi Dent J*. 2021;33(1):27–33. <https://doi.org/10.1016/j.sdentj.2019.11.008>
14. Tricco AC, Antony J, Zarin W, Striffler L, Ghassemi M, Ivory J, et al. A scoping review of rapid review methods. *BMC Med*. 2015;13(224). Available from: <https://doi.org/10.1186/s12916-015-0465-6>
15. Eldawlaty A, Alshehri H, Alqahtani A, Ahmad A, Al-Dammas F, Marzouk A. Appearance of Population, Intervention, Comparison, and Outcome as research question in the title of articles of three different anesthesia journals: A pilot study. *Saudi J Anaesth*. 2018 Apr-Jun;12(2):283–286. https://doi.org/10.4103/sja.SJA_767_17
16. Ohta K, Tada M, Ninomiya Y, ... Application of interconnected porous hydroxyapatite ceramic block for onlay block bone grafting in implant treatment: A case report. *Exp Ther Med* [Internet]. 2017;14:5564–8. <https://doi.org/10.3892/etm.2017.5224>
17. Stacchi C, Lombardi T, Oreglia F, Histologic and histomorphometric comparison between sintered nanohydroxyapatite and anorganic bovine xenograft in maxillary sinus grafting: A split-mouth randomized controlled clinical trial. *Biomed Res Int* [Internet]. 2017; <https://doi.org/10.1155/2017/9489825>
18. Nakata H, Kuroda S, Tachikawa N, Histological and micro-computed tomographic observations after maxillary sinus augmentation with porous hydroxyapatite alloplasts: a clinical case series. *Springerplus* [Internet]. 2016;5(260):1–8. <https://doi.org/10.1186/s40064-016-1885-2>
19. Maître G, Farias D, Moraes E de, Sacco R, Horizontal Ridge Augmentation of a Single Atrophic Site in the Anterior Maxilla Using Hydroxyapatite and rhBMP-2. *Int J Morphol* [Internet]. 2020;38(5):1426–33. <https://doi.org/10.4067/S0717-95022020000501426>
20. Resende RFB, Sartoretto SC, Uzeda MJ, Alves A, Randomized controlled clinical trial of nanostructured carbonated hydroxyapatite for alveolar bone repair. *Materials (Basel)* [Internet]. 2019;12:3645. <https://doi.org/10.3390/ma12223645>
21. Kattimani VS, Lingamaneni KP, Kreedapathi GE, Kattappagari KK. Socket preservation using eggshell-derived nanohydroxyapatite with platelet-rich fibrin as a barrier membrane: A new technique. *J Korean Assoc Oral Maxillofac Surg*. 2019;45(6):332–42. <https://doi.org/10.5125/jkaoms.2019.45.6.332>
22. Kijartom P, Thammarakcharoen F, The use of three dimensional printed hydroxyapatite granules in alveolar ridge preservation. *Key Eng Mater* [Internet]. 2017;751:663–7. <https://doi.org/10.4028/www.scientific.net/KEM.751.663>
23. Ohba S, Shido R, Asahina I. Application of hydroxyapatite/collagen composite material for maxillary sinus floor augmentation. *J Oral Sci*. 2021;63(3):295–7. <https://doi.org/10.2334/josnusd.21-0163>

24. Scarano A, Lorusso F, Oliveira PS de, Hydroxyapatite block produced by sponge replica method: mechanical, clinical and histologic observations. *Materials (Basel)* [Internet]. 2019;12:3079. <https://doi.org/10.3390/ma12193079>
25. H K, M A, M H. Maxillary sinus floor elevation using hydroxyapatite nano particles vs tenting technique with simultaneous implant placement: a randomized clinical trial. *Clin Implant Dent Relat Res*. 2019;21(6):1241–52. <https://doi.org/10.1111/cid.12859>
26. Altaweel AA, Baiomy A, Elsayed SAH. Effect of Nano-hydroxyapatite and platelet-rich fibrin covered by the amniotic membrane on osseointegration after mandibular piezoelectric ridge splitting [Internet]. *The Saudi Dental Journal*. Elsevier; 2021. <https://doi.org/10.1016/j.sdentj.2019.11.008>
27. Yamada M, Egusa H. Current bone substitutes for implant dentistry. *J Prosthodont Res*. 2018;62(2):152–61. <https://doi.org/10.1016/j.jpor.2017.08.010>
28. Viktorya Rstakyan, Liana Mkhitarian, Lilit Baghdasaryan, Tsovinar Ghaltaghchyan, Zaruhi Karabekian, Gohar Sevoyan, Marina Aghayan, Miguel A. Rodríguez. Stereolithography of ceramic scaffolds for bone tissue regeneration: Influence of hydroxyapatite/silica ratio on mechanical properties. *J of the Mechanical Behavior of Biomedical Materials*. 2024;152:106421. ISSN 1751-6161, <https://doi.org/10.1016/j.jmbbm.2024.106421>.
29. Gillman CE, Jayasuriya AC. FDA-Approved Bone Grafts and Bone Graft Substitute Devices in Bone Regeneration. *Mater Sci Eng C* [Internet]. 2021;130(September):112466. <https://doi.org/10.1016/j.msec.2021.112466>
30. Kökdere NN, Baykul T, Findik Y. The use of platelet-rich fibrin (PRF) and PRF-mixed particulated autogenous bone graft in the treatment of bone defect: An experimental and histomorphometrical study. *Dent Res J*. 2015;12(5):418–24. <https://doi.org/10.4103/1735-3327.166188>
31. Doonquah L, Holmes PJ, Ranganathan LK, Robertson H. Bone Grafting for Implant Surgery. *Oral Maxillofac Surg Clin North Am* [Internet]. 2021;33(2):211–29. Available from: <https://doi.org/10.1016/j.coms.2021.01.006>
32. Greenstein G, Cavallaro J. Implant insertion torque: Its role in achieving primary stability of restorable dental implants. *Compend contin educ dent*. 2017;38(2):88–95.
33. P. Dragonas, T. Katsaros, G. Avila-Ortiz, L. Chambrone, J.H. Schiavo, A. Palaiologou. Effects of leukocyte–platelet-rich fibrin (L-PRF) in different intraoral bone grafting procedures: a systematic review. *International J of Oral and Maxillofacial Surgery*. 2019; 48(2): 250-262. ISSN 0901-5027. <https://doi.org/10.1016/j.ijom.2018.06.003>