

Review Article

Carbonate apatite – A New Frontier in Biomaterials for Regeneration*Ashwini Balasubramani, Muthukumaraswamy Arunachalam, Vidhya Banu, Prabha P*

Department of Periodontology, Tamil Nadu Government Dental College and Hospital, Tamil Nadu. Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

(Received: 05-12-2025**Revised: 24-02-2026****Accepted: 02-03-2026)**Corresponding Author: *Ashwini Balasubramani* Email: *ashwininambiar1292@gmail.com***ABSTRACT**

Carbonate apatite (CO₃Ap) has evolved as a promising alloplastic bone graft material in periodontal and implant therapies due to its superior biological properties. Unlike hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP), CO₃Ap mimics the mineral composition of natural bone, with carbonate substitution improving its resorption by osteoclasts and promoting bone turnover. Fabricated via a dissolution–precipitation reaction using calcium carbonate (CaCO₃) precursors, CO₃Ap maintains structural integrity while avoiding thermal decomposition that occurs with other manufacturing processes. The low crystallinity, high specific surface area, and dense microstructure contribute to the enhanced osteoblast differentiation and bone matrix formation.

Histological studies have demonstrated CO₃Ap's superior bone regeneration capacity compared to HA and β-TCP, with faster healing and greater bone volume observed in animal models. Its honeycomb architecture further supports osteoconductivity by facilitating cellular activity and nutrient flow. CO₃Ap's versatility extends to applications in ridge augmentation, sinus lifts, and guided tissue regeneration. Coating titanium implants with CO₃Ap improves osseointegration and mechanical stability, while its mesoporous microspheres offer potential as drug carriers for antibiotics and bioactive molecules.

Despite its advantages, CO₃Ap faces limitations such as brittleness and high solubility. Future research aims to optimize its physicochemical properties and develop cost-effective fabrication methods. Composite materials incorporating CO₃Ap with polymers, collagen, or platelet concentrates may further enhance its clinical utility. Overall, CO₃Ap represents a significant advancement in bone grafting materials, with potential for widespread application in regenerative dentistry and tissue engineering.

Keywords: Carbonate Apatite; Bone Graft; Alloplast; Honey-Comb; Remodelling; CO₃ap Coated Implants; Intra-Bony Defect

1. INTRODUCTION

Periodontology's greatest power is that it continues to progress and adapt its focus on the basis of contemporary research spanning a vast range of scientific endeavour. Periodontitis is a chronic poly-microbial inflammatory disease-causing destruction of the supporting apparatus of the tooth. Reconstruction of the lost periodontium being the ultimate goal of every clinician, necessitates the aid of various therapeutic grafting modalities which helps in better soft tissue and hard tissue healing and induces regeneration of lost structures rather than only by scaling & root planing.

1.1 Bone grafts in regeneration

Periodontal regeneration is defined as the reproduction/reconstruction of lost or injured part in such a way that the architecture and function of lost or injured tissue is completely restored (glossary of periodontal term 1992). Regenerative medicine is one of the most important objectives of current rehabilitation therapies. To maintain the space for periodontal tissue regeneration, various bone graft substitutes have been applied.

Autogenous bone grafts have been considered the gold standard for bone grafting, owing to the properties of osteogenesis, osteoinductivity, and osteoconductivity. However, harvesting it

resulted in limited volume and required other surgical sites. Furthermore, its resorption rate is fast and the volume of periodontal tissue regeneration is unpredictable. From this point of view, using alternative bone graft materials like allogeneic, alloplastic and xenogenic bone grafts avoid the need to create a donor site. However, infections, immunogenic rejection, and the risk of disease transmission remains problems with allogenic and xenogenic bone grafting. To overcome these problems, various alloplastic bone graft materials have been developed for multiple clinical situations owing to their osteoconduction [1, 17].

1.2 Novel alloplastic material

The structure of the bone's extracellular matrix is made up of three primary components: a mineral phase, making up approximately 65% of its weight; an organic phase, constituting approximately 25% of its weight; and water, the remaining 10% of its weight. The mineral phase is composed of a hydroxyapatite(HA) variant known as dahllite, which exhibits poor crystallinity and nonstoichiometry. This form of hydroxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) contains many elemental replacements, including but not limited to magnesium and other ions. Among the substitutions, carbonate (CO_3) is the most common, accounting for approximately 3–8% by weight [2, 18]. The carbonate substituted form of hydroxyapatite is termed Carbonate apatite. The absorption properties of carbonate apatite (CO_3Ap) are affected by the content ratio of carbonate ion which reduce crystallinity within the apatite structure, thereby enhancing bone reformation or turnover. Importantly, CO_3Ap is absorbed solely by osteoclastic absorption; and, its absorption rate closely matches that of natural bone. Furthermore, the osteoconductivity of CO_3Ap is much higher than that of HA and beta tricalcium phosphate(β -TCP) [1, 19]. CO_3Ap is now available as an alloplastic material.

1.3 Fabrication of CO_3Ap

Bone apatite should be amenable as a grafting material. But the fabrication of CO_3Ap is challenging as it begins to decompose at 400°C

and cannot be manufactured by sintering without thermal decomposition or the release of carbondioxide (CO_2)

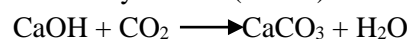
Recently, CO_3Ap blocks which are 100% chemically pure have been fabricated through a dissolution–precipitation reaction in an aqueous solution using a calcium carbonate(CaCO_3) block as a precursor [3].

The three requisites for compositional transformation through dissolution-precipitation reaction are:

- 1) Solubility of the precursor should be higher than that of final product.
- 2) Any component that is deficient must be supplied through aqueous medium.
- 3) The final product should have the ability to interlock to maintain shape of block.

The precursors for the fabrication of CO_3Ap through dissolution–precipitation reactions include CaCO_3 , α -tricalcium phosphate (α -TCP), dicalcium phosphate dihydrate(DCPD), and calcium sulphate (CaSO_4). When CaSO_4 is used as a precursor, sulphate ions continue to remain in the apatitic structure. CO_3Ap with a small amount of HA is formed on using α -TCP or DCPD due to the competitive reaction to form CO_3Ap and HA.

Since CaCO_3 has lower solubility at neutral pH in aqueous solution it is considered as one of the ideal precursors. CaCO_3 blocks which are chemically pure can be fabricated by exposing calcium hydroxide (CaOH) to CO_2 .



As phosphate is required for the compositional transformation of carbonate apatite from CaCO_3 , the blocks are immersed in phosphate salt solution [4].

1.4 CO_3Ap and bone remodelling:

Bone graft materials are used in regenerative procedures and implant treatment for optimizing functional and esthetic outcomes. The requirements for bone grafting materials should be that they must maintain the space for bone regeneration to occur and must be resorbed by osteoclasts and replaced with new bone tissue. Carbonate apatite granules are chemically synthetic bone allografts that are similar to autografts and more biocompatible than

allografts and xenografts[5]. It can be easily substituted for bone because its hydroxyl group is replaced with carbonate group, so a skeleton which has a porous microstructure that is morphologically similar to that of human cancellous bone is produced. CO_3Ap granules have shown greater bone formation in the cortical portion of bone defects than Bio-Oss, which is a xenograft. It has also demonstrated faster bone healing than HA *via* the activation of bone metabolism, which stimulates bone matrix formation by osteoblasts and bone absorption by osteoclasts. Bone remodelling - bone remodelling is the replacement of old bone or autograft through a process called resorption carried out by osteoclast, followed by formation or deposition of new bone by osteoblast.

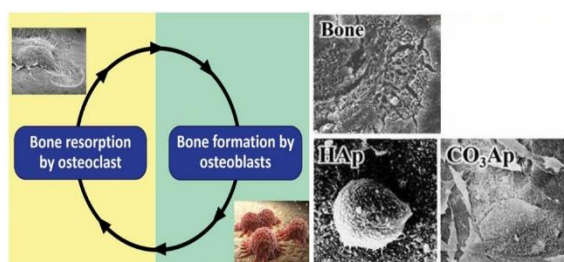


FIG1 (pic courtesy : Carbonate apatite artificial bone - Kunio Ishikawa and Koichiro Hayashi)

Carbonate apatite is osteoconductive. The osteoblasts are active on its surface but the degree of activity of both osteoblast and osteoclast depends on the type of crystals. Scanning electron microscopy (SEM) images of osteoclasts incubated on the surfaces of bone, HA, and CO_3Ap have showed osteoclastic resorption for bone and CO_3Ap whereas resorption was absent in HA.

Osteoclasts develop Howship's lacunae and decrease the pH inside it to 3–5, leading to the dissolution of bone apatite using a weak acid.

The activity of osteoblast is the counterpart of osteoclastic activity in bone remodelling. One among the determinants of osteoblastic activity is differentiation, the markers comprise of type I collagen, alkaline phosphatase (ALP), osteopontin, and osteocalcin. Human bone marrow cells (hBMCs) incubated on CO_3Ap have shown higher ex-pression than on HA. Amplification of osteoblast differentiation can be

considered one of the factors of the higher osteo-conductivity of CO_3Ap , in addition to their activation through cell-cell interactions with osteoclasts [4, 14].

2. Architecture of crystals

The infrastructure of crystals is also important in determining the features of artificial bone. Its regulation is considered key for artificial bone to demonstrate osteoconductivity similar to an autograft. One of the appealing architectures is the honeycomb. The honeycomb pattern is obtained by extrusion of raw material through a honeycomb die. An organic binder is necessary for extrusion and this must be eliminated subsequently by debinding [4].

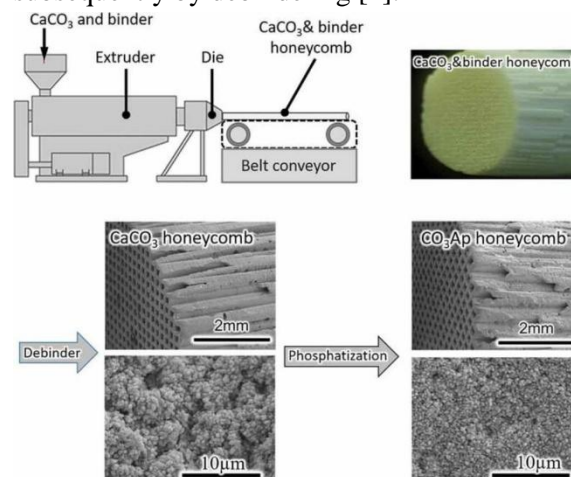


FIG 2 (Diagram of honeycomb fabrication process and SEM images of CaCO_3 and CO_3Ap honeycombs. Picture courtesy: Carbonate apatite artificial bone - Kunio Ishikawa and Koichiro Hayashi)

2.1 Physical properties

In a study done by Kunio Ishikawa *et al.*, comparing the physical characteristics of CO_3Ap , HA and β -TCP the following results were obtained [3, 20].

- 1) SEM showed both HA and β -TCP had porous structure. Conversely, CO_3Ap was dense. At higher magnification HA and β -TCP had smooth surfaces typical for sintering whereas, CO_3Ap surface was rough and had small precipitated crystals.
- 2) X ray diffraction studies revealed HA and CO_3Ap showing typical apatitic patterns with no other peaks. HA and β -TCP had sharp peaks, indicating high crystallinity, but

those of CO₃Ap were broad, indicating low crystallinity.

- 3) Crystallite sizes of HA and β-TCP were approximately 80 nm, whereas that of CO₃Ap was approximately 30 nm, which was smaller than half of HA.
- 4) Specific surface area (SSA) of HA was 1.0 m²/g and that of β-TCP was one order of magnitude smaller than HA and was 0.06 m²/g. By contrast, SSA of CO₃Ap was 18.2 m²/g which was one order of magnitude larger than HA.
- 5) Estimation of carbonate content revealed that it was 11.9 wt % in CO₃Ap and absent in HA and β-TCP,
- 6) Bulk density was largest for CO₃Ap and smallest for HA. On the other hand, HA had highest packing porosity followed by β-TCP and CO₃Ap.
- 7) At conditions similar to physiological pH, β-TCP showed the fastest dissolution rate followed by CO₃Ap and HA. Whereas in the weak acidic solution with pH 5.5 simulating the inside of the ruffle border of osteoclasts, CO₃Ap showed the fastest dissolution rate followed by β-TCP and HA.

2.2 Other general properties include [6]

- 1) It has a resorption time of 6-24 months.
- 2) 85% crystalline in nature.
- 3) Ca/p ratio – 1.67/1
- 4) pH 7.8
- 5) Carbonate apatite is resorbed by osteoclasts and the resorption rate accompanies the deposition of new bone tissue [5].
- 6) It also up-regulates osteoblast differentiation and demonstrates better osteoconductive properties than HA.
- 7) Carbonate apatite promotes bone deposition without fibrotic tissue formation.
- 8) Carbonate apatite is a non-hazardous and biocompatible material that aids osteoblast adhesion and proliferation.

Histological studies [3].

HA, β-TCP and CO₃Ap implanted into dog mandibular bone defect and studied histologically at 4, 8 and 12 weeks after implantation revealed the following:

- 1) Bone formation and resorption of bone substitute is different according to the type of bone substitute.
- 2) The highest bone amount was observed at both 4 and 12 weeks in the defects reconstructed with CO₃Ap.
- 3) Larger amounts of bone were observed at 12 weeks than that at 4 weeks, regardless of the type of bone substitute.

3. Uses

- 1) Augmentation or reconstructive treatment of the alveolar ridge.
- 2) Filling of periodontal defects.
- 3) Filling of defects after root resection, apicectomy, and cystectomy.
- 4) Filling of extraction sockets to improve preservation of the alveolar ridge.
- 5) Elevation of the maxillary sinus floor.
- 6) Filling of periodontal and peri-implant defects in conjunction with products intended for Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR).

4. Advantages

- Previous studies have demonstrated the presence the CD31 positive endothelial cells around the carbonate apatite material. This may be due to the blood flow and the abundant supply of nutrients that result from angiogenic processes. These findings strongly suggest that the faster bone formation observed in the CO₃Ap transplants was due to the promotion of angiogenesis [7, 15].
- CO₃Ap is an effective and suitable bone substitute material for faster bone healing, that is accompanied by recruitment of osteoclasts and endothelial cells, as compared with other alloplastic materials.
- Current data indicate that CO₃Ap is a predictable bone graft material for the treatment of vertical bone defects caused by periodontitis.
- Titanium (Ti) is used as an implant material due to its high mechanical strength and ease of osseointegration. But the osteogenesis of even surface roughened Ti, is poorer than

other osteoconductive materials like apatite. Therefore, premature loosening of Ti implants is a problem for early loading. Therefore, implants that are Ti roughened and surface coated with CO₃Ap can be an ideal choice because of its superior osteoconductivity [8, 16].

- The properties of this Ti implant material can be improvised through co-substitutions of CO₃ and other ions with concentrations equal to those in the physiological conditions. Some co-substitutions have recently been reported, using carbonate ions along with magnesium, yttrium, sodium, strontium, or silicate ions. Coatings of manganese substituted CO₃Ap have shown improved activation of metabolism, osteoblast differentiation, and proliferation [11].
- In addition, to improving the mechanical and biological properties of implants CO₃Ap coatings on it may also be loaded with bioactive molecules to serve as carriers[13].
- Micron and mesoporous CO₃Ap microspheres have showed excellent drug loading efficiency. Several studies have demonstrated that CO₃Ap could be used as a carrier for aminoglycosides. Mesoporous microspheres of CO₃Ap when used for controlled delivery of gentamycin and vancomycin exhibited excellent biocompatibility, antibacterial properties, and it also efficiently prevented the adhesion of *Staphylococcus epidermidis* [12].



FIG 3 Medical applications of carbonate apatite (pic courtesy - Biological Properties and Medical Applications of Carbonate Apatite: A Systematic Review)

5. Future thoughts

The field of material science and tissue engineering are swiftly progressing, permitting for improved bone regeneration.

Carbonate apatite is a ceramic material that has shown promising biological properties and, thus, can be considered as a supreme bone grafting material of choice in the future.

However, it has some limitations, which includes its inferior mechanical properties (brittleness and unsatisfactory fatigue resistance) and rapid solubility. Modifications of its physicochemical characteristics (e.g., pore size, crystallinity, interconnectivity of the pores, carbonate content) can help to successfully adapt the material for the specific needs of certain applications [8].

Another limitation of CO₃Ap is its challenging and expensive fabrication. Efforts have been directed towards the establishment of more efficient and economical fabrication protocols²¹. The application of nano carbonate apatite (n-CAP) based dentifrice after non-surgical periodontal therapy had some benefit on the reduction of dentin hypersensitivity after 4-week at home use [9].

Similar to other calcium phosphate ceramics, CO₃Ap can be used in various composite materials, including CO₃Ap/polymers, CO₃Ap/chitosan, CO₃Ap/collagen, CO₃Ap/autologous platelet concentrates, and so on [10].

Furthermore, this material has great loading potential and should be assessed as a carrier for biologically active substances, such as drugs, BMPs, growth factors, stem cells, and so on [11].

6. Conclusion

The rising need for bone grafting materials with enhanced properties has led to the introduction of carbonate-containing apatites. This material has exhibited excellent biocompatibility, bioresorbability, bioactivity, and osteoconductivity, permitting rapid bone replacement and maturation. However, some of its major limitations, are poor mechanical properties and high solubility. These can be compensated by modification of its physicochemical properties.

Carbonate apatite has already exhibited supremacy over other alloplastic bone substitutes like HA and β -TCP and scaffold materials. Furthermore, it can be used for the synthesis of biomimetic, composite materials, and co-substituted apatites that show enhanced mechanical, biological properties, and tissue behavior. Carbonate apatite can be used in tissue engineering, serving as a potential bioactive coating and/or a drug-delivery system. Further preclinical and long-term clinical trials are necessary to substantiate the safety and efficacy of this material, and to validate its recently disclosed supremacy over other largely used bioceramics. The available scientific literature has shown promising results in this regard.

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Conflict of Interest

“We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.”

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Ethical Information

This article does not involve studies with human participants or animals performed by any of the authors. Therefore, ethical approval and informed consent were not required.

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