IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736.Volume 17, Issue 1 Ser. I (January 2024), PP 56-64
www.iosrjournals.org

Hydroxyapatite Production Techniques: Overview Of Precipitation, Sol-Gel, Hydrothermal, And Thermal Decomposition Methods

Suleyka Torres-Romero[1,2], Alexander Mendoza-Acosta[2,3], M.R. Flores-Cortez[1], F. Gamez-Serna[1], A.S. Váldez-Robles[1],C.A. Soto-Robles[1]

[1]Universidad Autónoma Indígena de México,[2]Tecnológico Nacional de México/IT De Los Mochis, C.P.81259, Los Mochis, Sinaloa, México, [3]Faculty Of Economics, National Autonomous University Of Mexico.

Abstract
The development of industrial activity, subject to rapid growth in recent years, has successfully met multiple societal needs while making products and services more accessible to the population. However, the high use of raw materials, consumption of substantial amounts of energy, and the generation of byproducts, waste, and pollutants have created significant imbalances in the economy and the environment. In response to these negative changes, the circular economy emerges as an imperative need in the production of goods and services. Therefore, it is important to identify processes that utilize both waste and byproducts from other industrial processes, allowing the integration of these materials into the value chain. On the other hand, the demand for biocompatible materials has exponentially increased due to awareness of their importance and recent advances in material technology, enabling the production of materials with specific characteristics. Among these materials, hydroxyapatite (HAp) stands out as a commercially important biomaterial. This is attributed to its potential to be obtained from bone waste, scales, and/or exoskeletons of animals, as well as its wide range of applications, covering everything from dental prosthetics to water treatment and polymer production. Given the aforementioned, this article summarizes four common techniques used to obtain hydroxyapatite, including chemical precipitation, thermal decomposition, hydrothermal method, and sol-gel method.

Keywords:*Hydroxyapatite; Waste materials; Biomaterials; Synthesis Methods.*

Date of Submission: 20-01-2024 Date of Acceptance: 30-01-2024

I. Introduction

Hydroxyapatite (HAp) is a mineral compound essentially made up of calcium phosphate, whose crystalline structure can take various forms from pillar to spherical structures, passing through column and plate type, due to the importance of its crystal lattice this has been studied for several decades, as shown by the work of Hendriks and his team of collaborators, from which one of the crystal structure configurations for hydroxyapatite can be presented (Figure 1).(Hendricks, Jefferson, & Mosley, 1932)

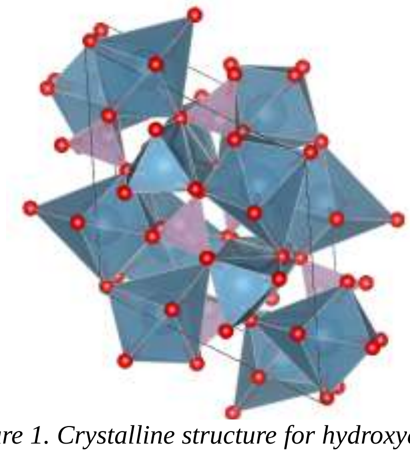

Figure 1. Crystalline structure for hydroxyapatite

This compound, with the general formula Ca10(PO4)$_6$(OH)$_2$, is the main mineral phase present in bone tissue. Because of its similarity to the natural components of bones and teeth, hydroxyapatite has gained increasing attention in various biomedical applications, including the manufacture of bone implants, prosthetic coatings, and bone regeneration materials. Likewise, the processes of obtaining hydroxyapatite have experienced remarkable progress in recent decades, driven by the growing demand for biocompatible materials in tissue engineering, bone regeneration and dentistry. One promising avenue for sustainably sourcing biomaterials is to explore natural sources and waste as precursors. (Pokhrel, 2018) (Alif, 2018) (Hussin, 2022)

Natural sources, from which HAp can be extracted, reported by Verma (2023) range from plants, minerals, and animals, including algae. From terrestrial and marine animals, it is obtained from bones, scales, shells, and shells of mollusks. The above-mentioned feedstock sources are rich in calcium carbonate, an essential precursor for hydroxyapatite. Currently, the need to synthesize HAp in an efficient and ecologically friendly way has increased, so preparation methods are constantly expanding and improving.

So far, groundbreaking research has been conducted to obtain adaptable shapes, uniform composition, specific surface area, fine grain, better performance, and many perfect HAp crystal conditions. The process for obtaining them involves the extraction of these natural materials and their transformation through chemical or hydrothermal precipitation methods. Not only does this approach use renewable resources, but it also minimizes reliance on unsustainable mineral sources.(Verma, 2023)(Afriani, 2020)

The conversion of waste into hydroxyapatite usually involves a process of chemical precipitation. The calcium carbonate present in the waste undergoes controlled chemical reactions that transform the crystal structure into hydroxyapatite. This process can be carried out using various techniques, such as hydrothermal, sol-gel, or precipitation at room temperature.

The choice of the method will depend on factors such as the desired purity of the final product, the efficiency of the process and the available resources, which is why this article compiles a review related to some methods for obtaining hydroxyapatite using natural sources as raw material, more specifically marine debris from the Pacific coast.

Methods for obtaining HAP.

Chemical Precipitation and Thermal Decomposition

Chemical precipitation is one of the most common methods for obtaining hydroxyapatite. It involves the controlled mixing of calcium and phosphate salt solutions, resulting in the formation of hydroxyapatite crystals. Ahmed (2022) reports the synthesis of hydroxyapatite conducted by the technique of calcination and wet chemical precipitation. Briefly, it dropped phosphoric acid (0.6 M, H_3PO_4) to calcium hydroxide ($Ca(OH)_2$) at a rate of 15 to 20 drops/min with continuous stirring at room temperature to produce hydroxyapatite (see eqn. 1).

$$10\ Ca(OH)_2 + 6\ H_3PO_4 \rightarrow Ca_{10}\ (PO4)_6\ (OH)_2 + 18H_2O \quad \text{Eqn. 1}$$

Subsequently, ammonium hydroxide (NH_4OH) solution was added until the reaction was complete, the pH was maintained around 8 for about 2 hours, and the solution was constantly stirred, this helps to improve the HAp production as shown in chemical equations 2 and 3. A gelatinous white precipitate was obtained after the solution stopped stirring and was allowed to precipitate overnight. The solution was filtered and rinsed four times with distilled water before being dried at 200°C for 24 h to remove the water.

$$12\ NH_4OH + 6\ H_3PO_4 \rightarrow 6\ (NH_4)_2HPO_4 + 12\ H_2O \quad \text{Eqn. 2}$$
$$10\ Ca(OH)_2 + 6\ (NH_4)_2HPO_4 + 2\ H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 12\ NH_4OH + 8\ H_2O \quad \text{Eqn. 3}$$

Finally, the hydroxyapatite obtained was sintered in the furnace at a temperature of 1000°C for 4 hours. The resulting hydroxyapatite was characterized by XRD, EDX, and FT-IR. Although this method is straightforward, the purity of the product and the manipulation of the reaction conditions are overly sensitive to ensure the quality of the material.Apkan et al. (2020), in their study, report variation in calcination temperature, 900°C, 1000°C and 1100°C, to evaluate the properties of HAp produced from two biogenic sources and found that the properties of HAp, such as hardness and resistance to breakage, vary with respect to the source and the applied temperature (Ahmed, 2022), this could be explained by the thermal reconfiguration of the crystalline structure.

Thermal decomposition involves the calcination of phosphate and calcium precursors at elevated temperatures. This method is effective in obtaining high-purity hydroxyapatite, but temperature control and exposure time are especially important to prevent the formation of unwanted secondary phases.

Figure 2 shows a basic flowsheet for the chemical precipitation process, it should be noticed that reactions can be conducted with different reactants, but the process is the same.

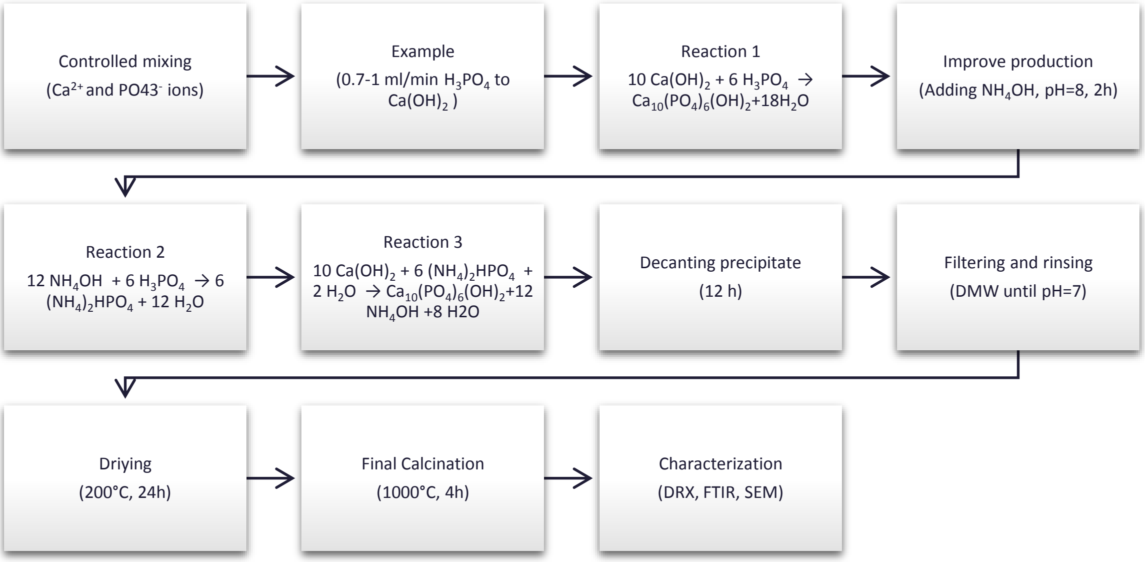

Figure 2. Chemical precipitation process for HAP production

Hydrothermal process

Hydrothermal synthesis is a method that is noted for its ability to control the particle size and morphology of hydroxyapatite crystals. Alif et al. (2018), have used a hydrothermal method for HAp synthesis, using waste materials from freshwater clam shells. The clam shells were calcined at different temperatures (900 and 1000°C) for 5 hours, at this stage, they were transformed into calcium oxide (see eqn. 4) releasing carbon dioxide.

$CaCO_3 \rightarrow CaO + CO_2$ *Eqn. 4*

The resulting calcium oxide was then converted to calcium hydroxide $Ca(OH)_2$ through a hydration process, according to chemical equation 5, by letting the metal oxide come into contact with the air by placing it in a moist location for a week.

$CaO + H_2O \rightarrow Ca(OH)_2$ *Eqn. 5*

For synthesis, a stoichiometric value of ammonium dihydrogen phosphate (sodium dihydrogen phosphate could be used) was dissolved in distilled water and added to 10 g of the pyrolyzed shells, continuously mixing at a rate of 300 rpm and the temperature was maintained at approximately 90°C for 6 h (see eqn. 6 and 7). After heating, the slurry was dried at 120°C for 5 h and calcined at 600°C for 2 h.

$10\ Ca(OH)_2 + 6\ NaH2PO4 \rightarrow Ca10(PO4)_6(OH)_2 + 12\ H2O + 6\ NaOH$ *Eqn. 6*

$10\ Ca(OH)_2 + 6\ (NH4)H2PO4 \rightarrow Ca10(PO4)_6(OH)_2 + 12\ H2O + 6\ NH4OH$ *Eqn. 7*

Through the hydrothermal method, Afriani (2020) also reports the production of hydroxyapatite from tuna bones, with the variation that, after calcination, the mixture of CaO powder from tuna bones obtained and ammonium dihydrogen phosphate solution was heated in an autoclave to 900°C to produce hydroxyapatite powder, Although the author indicates that this method has a weakness, in addition to hydroxyapatite, it can also produce fluorapatite.

The shells of various animals, such as crabs, have been used as raw materials due to their calcium-rich content. The synthesis is conducted by the wet deposition method, previously subjected to calcination to generate CaO or $Ca(OH)_2$ and reacted with water, mixed with an H_3PO_4 solution followed by sintering at 900°C for 2 hours (see eqn. 8). (Afriani, 2020)

$10\ Ca(OH)_2 + 6\ H_3PO_4 \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 18H_2O$ *Eqn. 8*

The basic flowsheet for this process is shown on figure 3.

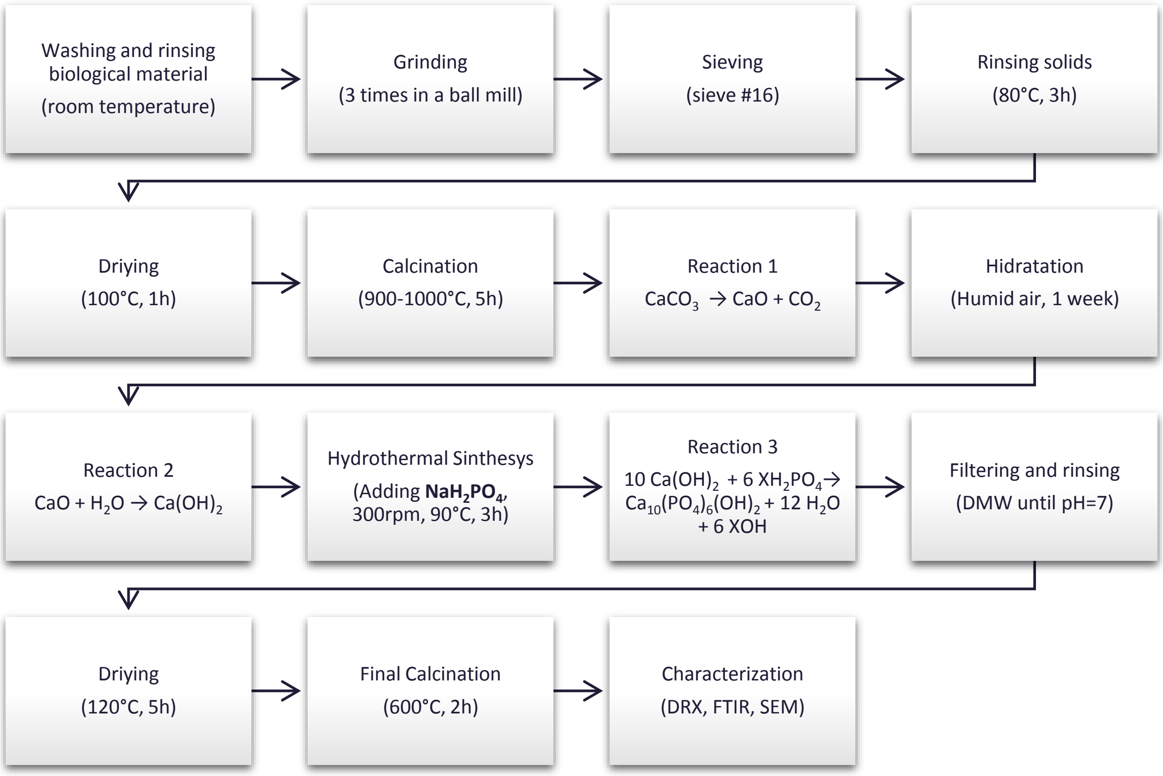

Figure 3. Hydrothermal process for HAP production

Sol-Gel

The sol-gel method offers exceptional control over the composition and morphology of hydroxyapatite, being an advantage at the molecular level of the mixture of calcium and phosphorus precursors and is able to improve the results of HAp chemical homogeneity to a significant degree, compared to conventional techniques, this method consists of starting with a colloidal solution that then forms a gel, achieving a structural homogeneity that can be crucial in tissue engineering applications. However, manipulation of synthesis parameters is essential to prevent the formation of unwanted phases. (Azis, 2018)

The sol-gel method has been widely applied in the synthesis of HAp from synthetic precursors, Rangel et. al. (2019) obtained HAp from solutions of calcium nitrate tetrahydrate ($Ca(NO_{3)2}$•$4H_2O$), sodium phosphate (Na_3PO_4) and sodium hydroxide (NaOH), first mixing the solutions of Na_3PO_4 and NaOH in a sonicator for 5 minutes, The mixture was then placed in an injection syringe, which added the $Ca(NO_3)_2$•$4H_2O$ solution to a 40 ml/h cup (see eqn. 9). The precipitate was washed, filtered, and dried for 24 h at 80°C.

$10\ Ca(NO_3)_2 \bullet 4H_2O + 6\ Na_3PO_4 + 2NaOH \rightarrow Ca_{10}(PO_4)6(OH)_2 + 20NaNO_3 + 4\ H_2O$ *Eqn. 9*

The schematic process for this method is shown in figure 4.

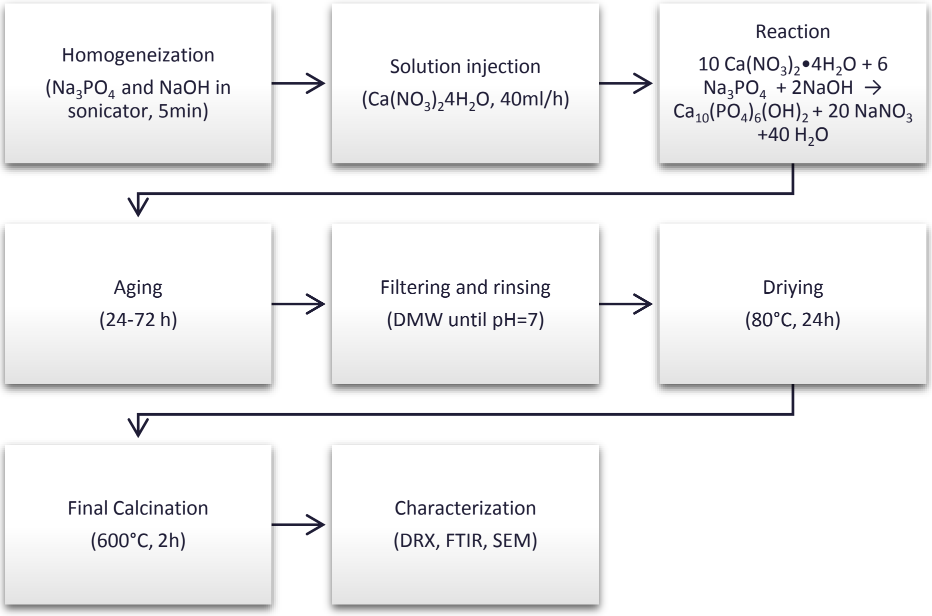

Figure 4. Sol-Gel process for HAP production using synthetic precursors.

Azis et al. (2018) used eggshells for hydroxyapatite synthesis using the sol-gel method, varying aging time (24, 48, 72 h), molar ratio of Ca and P (1.57; 1.67 and 1.77) and pH (9, 10, 11). The method consisted of mixing a solution of calcium carbonate previously dissolved in 0.3M nitric acid with a solution of $(NH_4)_2HPO_4$ in a beaker. The solution was stirred for 3 h at a stirring speed of 300 rpm until the gel was formed (see eqn. 10 and 11). The formed gel is dried in the oven at 80 °C for 24 hours. The solids obtained were cleanly washed with distilled water to separate the hydroxyapatite from the rest of the reagents and dried for 3 h in the oven. Finally, the solids obtained were calcined for 1 hour at 500 °C.

$CaCO_3 + HNO_3 \rightarrow Ca(NO_3)_2 + CO_2 + H_2O$ *Eqn. 10*
$10\ Ca(NO_3)_2 + 6\ (NH_4)_2HPO_4 + 2\ H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 12\ NH_4NO_3 + 8\ HNO_3$ *Eqn. 11*

Figures 5 and 6 show the schematic flowsheet for different process using this method.

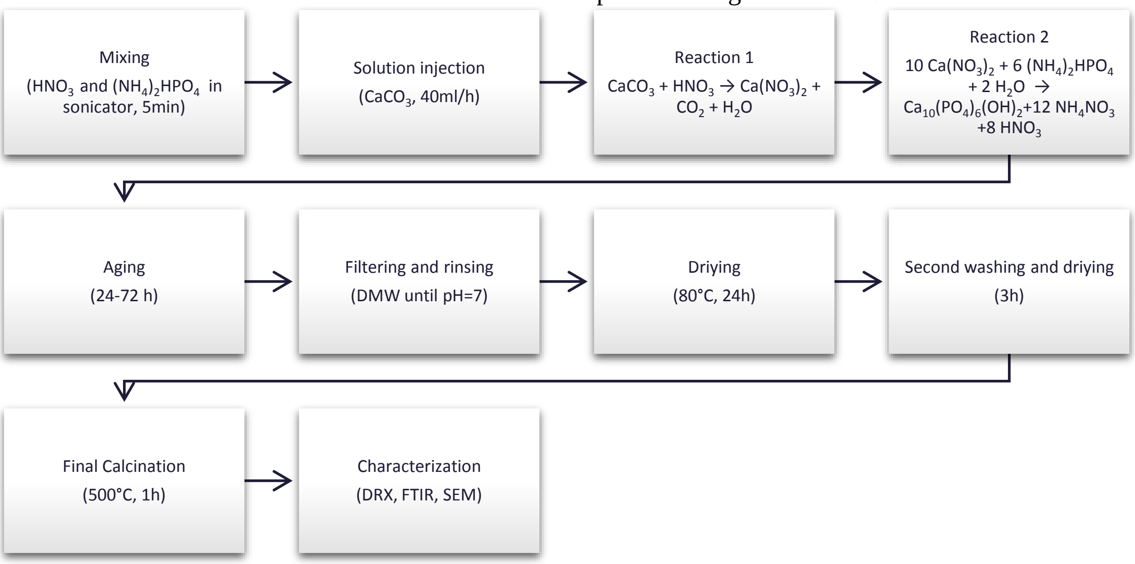

Figure 5. Sol-Gel process for HAP production using organic waste.

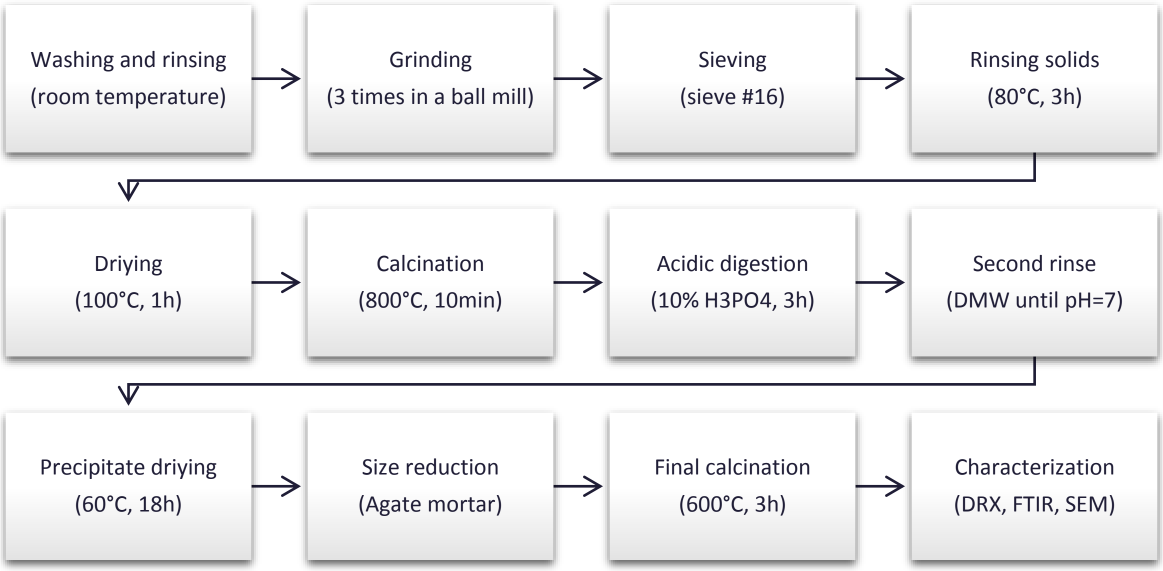

Figure 6. Sol-GEL process for PAH production using marine animal exoskeletons.

Technical Comparison

Given the variability in both production processes and the raw materials selected for the chemical synthesis of hydroxyapatite, it is not possible, at least in a general sense, to perform a quantitative technical comparison. However, by studying the parameters and techniques collectively for each method, a qualitative comparison can be made, allowing for a more appropriate evaluation of the different chemical routes for the synthesis of this compound of interest.

Table 1 provides a summary of the key parameters for each synthesis method:

Table 1 Main process parameters for distinct methods for HAP production

Synthesis Method	*Temperature*	*Raw Materials*	*Control*	*Crystal size*	*Selectivity*	*Yield*	*Cost level*
Precipitation	Moderate to High	Calcium and phosphate precursors, often salts.	pH, aging time, temperature	400-600 nm	Limited control over morphology; generally high selectivity	Moderate to High, cost-effective	Low to Moderate
Sol-Gel	Moderate to High	Colloidal solution, calcium, and phosphorus precursors	Composition and morphology at the molecular level, pH, temperature	200-400 nm	Excellent control at the molecular level; high selectivity	Moderate, requires careful parameter manipulation	Moderate to High
Hydrothermal	High	Calcium and phosphate precursors, often salts	Temperature, pressure	300-600 nm	Excellent control over particle size and morphology	Moderate, relatively energy-intensive	Moderate to High
Thermal Decomposition	Very High	Calcium and phosphate precursors, often salts	Temperature, exposure time	400-600 nm	Effective in obtaining high-purity hydroxyapatite	High, but careful temperature control is required	High

In the upcoming lines, a basic SELECT analysis for the chemical route selection of hydroxyapatite synthesis methods will be performed. The SELECT framework, encompassing Safety, Environment, Legal, Economy, Control, and Throughput parameters, allows us to comprehensively evaluate and compare these methods based on key criteria. Each parameter will be assigned a subjective rating from 0 to 10 for four synthesis methods: Precipitation, Sol-Gel, Hydrothermal, and Thermal Decomposition. These ratings aim to provide a qualitative assessment of the safety, environmental impact, legal considerations, economic efficiency, control capabilities, and overall throughput of each method. The analysis will assist in making informed decisions regarding the most suitable chemical route for hydroxyapatite synthesis based on the specified evaluation criteria.

Safety:

The safety considerations for the synthesis methods vary based on the processes involved. In the Precipitation method, which employs acids or bases such as phosphoric acid or ammonia, safety risks are moderate. The reactions typically occur at moderate temperatures (around 60-80°C) and atmospheric pressure, contributing to a generally safe and efficient process. The Sol-Gel method, using colloidal solutions like alkoxides, has a low safety risk due to lower temperatures (around 40-80°C) and ambient pressure. Both these methods provide a level of safety suitable for laboratory and industrial applications.

The Hydrothermal method introduces higher safety concerns due to the involvement of high pressure (typically above 1 MPa) and elevated temperatures (around 150-200°C). Despite these challenges, proper handling measures can mitigate risks. Lastly, the Thermal Decomposition method involves extremely elevated temperatures (above 800°C), presenting a moderate to high safety risk. Stringent safety protocols and precise temperature control are essential for the safe execution of this method.

Environment:

Environmental impact is a critical factor in the comparison of hydroxyapatite synthesis methods. The Precipitation method, using acids or bases, generally has a moderate environmental impact. The reactions occur at moderate temperatures and atmospheric pressure, minimizing environmental risks. The Sol-Gel method, utilizing colloidal solutions, also has a moderate environmental impact due to its relatively mild reaction conditions.

On the other hand, the Hydrothermal method may have a higher environmental impact, primarily due to its energy-intensive nature. The high pressure and temperature conditions, while effective in controlling particle size, can contribute to increased energy consumption. The Thermal Decomposition method, involving extremely elevated temperatures, also poses moderate environmental concerns. Careful management of energy usage and waste disposal is crucial for minimizing environmental impact in both these methods.

Legal:

All four hydroxyapatite synthesis methods face no specific legal restrictions. The use of acids, bases, and other common chemicals in these processes does not typically raise legal concerns. Researchers and industrial practitioners can proceed with these methods without encountering legal obstacles.

Economy:

Economic efficiency is a key consideration in the selection of a synthesis method. The Precipitation method is often considered cost-effective. Its use of acids or bases, moderate temperatures, and atmospheric pressure contribute to a relatively low-cost process. The Sol-Gel method, while providing excellent control and moderate to high throughput, tends to have a moderate to prohibitive cost due to the use of colloidal solutions.

The Hydrothermal method and Thermal Decomposition method both involve higher costs. Hydrothermal synthesis, with its high pressure and temperature requirements, may lead to increased energy consumption, impacting overall economic efficiency. Thermal decomposition, requiring extremely elevated temperatures, is energy-intensive, contributing to higher costs.

Control:

Control over the synthesis process is determinant for achieving desired hydroxyapatite properties. The Precipitation method offers moderate control over morphology and composition, with the formation of hydroxyapatite crystals at moderate temperatures and atmospheric pressure. The Sol-Gel method provides excellent control at the molecular level, allowing for precise management of composition and morphology.

The Hydrothermal method excels in control over particle size and morphology, thanks to high pressure and temperature conditions. The Thermal Decomposition method, while effective in obtaining high-purity hydroxyapatite, provides moderate control over the synthesis parameters.

Throughput:

Throughput, representing the efficiency of the synthesis process, varies among the methods. The Precipitation method boasts a high throughput, as the reactions occur at moderate temperatures and atmospheric pressure. The Sol-Gel method offers moderate to high throughput, considering the meticulous control it provides at the molecular level.

The Hydrothermal method provides a moderate throughput due to the energy-intensive nature of the process. The Thermal Decomposition method also offers a moderate throughput, influenced by the remarkably elevated temperatures required.

Due to the previously stated information, the selection of a hydroxyapatite synthesis method depends on the specific requirements of the application, considering factors such as safety, environmental impact, economic efficiency, control, and throughput as well as crystal size and raw materials availability. Each method has its strengths and challenges, and the choice should align with the desired outcomes and available resources.

Table 2 provides subjective ratings for the processes discussed in this paper. It is important to notice that these ratings serve only as a general guide. Conducting a detailed analysis for specific methods (rather than a family of methods) is essential to accurately assess their feasibility and rank them in comparison to one another. The ratings in the table offer initial orientation, emphasizing the need for a more nuanced evaluation tailored to the unique characteristics and requirements of individual synthesis methods.

Table 2 SELECT criteria for selection from distinct methods for HAP production.

Synthesis Method	Safety	Environment	Legal	Economics	Control	Throughput	Average
Precipitation	7	7	10	8	6	8	7.7
Sol-Gel	9	8	10	6	9	7	8.2
Hydrothermal	5	6	10	5	9	6	6.8
Thermal Decomposition	5	6	10	4	6	6	6.2

II. Conclusions

Advancements in hydroxyapatite production processes have ushered in new prospects for biomaterial manufacturing. The array of available methods enables tailoring hydroxyapatite properties to suit diverse requirements in medical and tissue engineering applications. The conclusions drawn from the SELECT analysis, integrating Safety, Environment, Legal, Economy, Control, and Throughput parameters for various synthesis methods, shed light on the nuanced strengths and challenges associated with each approach. This comprehensive understanding is critical for informed decision-making in selecting the most suitable chemical route for hydroxyapatite synthesis. As research progresses, enhancing the efficiency of current methods and uncovering innovative approaches hold the promise of significant strides in hydroxyapatite synthesis. This, in turn, sets the stage for the development of advanced and personalized biomaterials, propelling advancements in tissue regeneration and repair.

Moreover, the utilization of waste materials for biomaterial production materializes as a promising and sustainable strategy. This not only addresses concerns surrounding waste management but also offers an eco-friendly alternative for obtaining essential biomaterials across diverse domains. Ongoing research efforts not only drive the evolution of more efficient technologies but also contribute substantively to the development of sustainable solutions, attending both environmental and medical challenges of our time. The pursuit of these sustainable strategies aligns with the broader goal of fostering environmentally conscious practices within the realm of biomaterial production and medical applications.

Acknowledgements

The authors extend their sincere gratitude to the Tecnológico Nacional de México for their invaluable support of the project titled "Use of Exoskeletons of Marine Species to Obtain Hydroxyapatite" (17748.23-P) under the 2023 Call for Scientific Research Projects, Technological Development, and Innovation. This support has been instrumental in advancing our research endeavors, contributing to the exploration of innovative methodologies in the synthesis of hydroxyapatite from marine exoskeletons. The authors deeply appreciate the institution's commitment to fostering scientific excellence and technological innovation.

References

[1]. Afriani, F. S. (2020). Hydroxyapatite From Natural Sources: Methods And Its Characteristics. Iop Conference Series: Earth And Environmental Science, 599(012055). Doi:10.1088/1755-1315/599/1/012055

[2]. Ahmed, H. Y. (2022). Synthesis Of Natural Nano-Hydroxyapatite From Snail Shells And Its Biological Activity: Antimicrobial, Antibiofilm, And Biocompatibility. Membranes, 12(4), 408. Doi:Http://Dx.Doi.Org/10.3390/Membranes12040408

[3]. Akpan, E. D.-A. (2021). Hydroxyapatite Ceramics Prepared From Two Natural Sources By Direct Thermal Conversion: From Material Processing To Mechanical Measurements. Materials Today: Proceedings, 2291-2294. Retrieved From Https://Doi.Org/10.1016/J.Matpr.2020.06.391.

[4]. Alif, M. A. (2018). A Hydrothermal Synthesis Of Natural Hydroxyapatite Obtained From Corbicula Moltkiana Freshwater Clams Shell Biowaste. Materials Letters, 230, 40-43. Doi:Https://Doi.Org/10.1016/J.Matlet.2018.07.034

[5]. Azis, Y. A. (2018). Synthesis Of Hydroxyapatite Nanoparticles From Eggshells By Sol-Gel Method. Iop Conference Series: Materials Science And Engineering, 354. Doi:Doi:10.1088/1757-899x/345/1/012040

[6]. Gunduz, O. S.-N. (2014). A New Method For Fabrication Of Nanohydroxyapatite And Tcp From The Sea Snail Cerithium Vulgatum. Journal Of Nanomaterials, 382861. Doi:10.1155/2014/382861

[7]. Hernández, K. L. (2022). Hydroxyapatite Recovery From Fish Byproducts For Biomedical Applications. Sustainable Chemistry And Pharmacy, 28(100726). Doi:Https://Doi.Org/10.1016/J.Scp.2022.100726.

[8]. Hussin, M. A. (2022). Extraction Of Natural Hydroxyapatite For Biomedical Applications - A Review. Heliyon, 08(08), E10356. Retrieved From Https://Www.Sciencedirect.Com/Science/Article/Pii/S2405844022016449

[9]. Pokhrel, S. (2018). Hydroxyapatite: Preparation, Properties And Its Biomedical Applications. Advances In Chemical Engineering And Science, 8(4), 225-240. Doi:Https://Doi.Org/10.4236/Aces.2018.84016

[10]. Rangel, V. G. (2019). Synthesis Of Hydroxyapatite And Fluorapatite. Trends In Teaching And Research In Chemistry, 5(5), 295-300. Retrieved From Http://Hdl.Handle.Net/11191/7833

[11]. Verma, R. M. (2023). Hydroxyapatite-Based Composites: Excellent Materials For Environmental Remediation And Biomedical Applications. Advances In Colloid And Interface Science, 315(102890). Doi:Https://Doi.Org/10.1016/J.Cis.2023.102890