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GREEN SYNTHESIS OF HYDROXYAPATITE FROM BIOGENIC AND WASTE-DERIVED PRECURSORS: A BIBLIOMETRIC AND SYSTEMATIC ANALYSIS OF TRENDS, STRATEGIES, AND APPLICATIONS

SÍNTESE VERDE DE HIDROXIAPATITA A PARTIR DE PRECURSORES BIOGÊNICOS E DERIVADOS DE RESÍDUOS: UMA ANÁLISE BIBLIOMÉTRICA E SISTEMÁTICA DE TENDÊNCIAS, ESTRATÉGIAS E APLICAÇÕES

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ABSTRACT

This study presents a comprehensive bibliometric and qualitative analysis of the scientific literature on the green synthesis of hydroxyapatite (HAp) derived from biogenic and waste-based precursors. The dataset was retrieved from the Scopus database and analyzed using a structured workflow, including screening, eligibility assessment, and bibliometric mapping. The results reveal a consistent growth in scientific production, particularly after 2023, indicating the increasing relevance of sustainable synthesis strategies. Geographic analysis highlights a strong concentration of research in emerging economies, especially in Asia. Keyword and co-occurrence analyses demonstrate that the field is structured around four main domains: green synthesis approaches, material development, physicochemical characterization, and application-driven research. The most influential studies emphasize the use of calcium-rich waste materials, bio-mediated synthesis routes, and the development of hybrid and multifunctional systems. Furthermore, the qualitative analysis evaluates the underlying physicochemical and kinetic mechanisms of these green pathways, demonstrating how alternative synthesis methods operate as efficient crystal engineering strategies. Additionally, HAp-based materials are increasingly applied in both biomedical and environmental contexts, including bone tissue engineering and pollutant removal. Despite these advances, challenges remain regarding reproducibility, standardization, and scalability of green synthesis methods. Overall, this study provides a structured and integrative overview of the field, identifying key trends, research gaps, and future directions toward more sustainable and high-performance HAp-based materials.

Keywords: Biomaterials; Bone Tissue Engineering; Circular Economy; Nanostructured Materials; Waste Valorization.

RESUMO

Este estudo apresenta uma análise bibliométrica e qualitativa abrangente da literatura científica sobre a síntese verde de hidroxiapatita (HAp) derivada de precursores biogênicos e de resíduos. O conjunto de dados

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foi obtido na base Scopus e analisado por meio de um fluxo de trabalho estruturado, incluindo triagem, avaliação de elegibilidade e mapeamento bibliométrico. Os resultados revelam um crescimento consistente da produção científica, especialmente após 2023, indicando a crescente relevância das estratégias de síntese sustentável. A análise geográfica destaca uma forte concentração de pesquisas em economias emergentes, particularmente na Ásia. As análises de palavras-chave e de coocorrência demonstram que o campo está estruturado em quatro domínios principais: abordagens de síntese verde, desenvolvimento de materiais, caracterização físico-química e pesquisas orientadas à aplicação. Os estudos mais influentes enfatizam o uso de materiais residuais ricos em cálcio, rotas de síntese mediadas por agentes biológicos e o desenvolvimento de sistemas híbridos e multifuncionais. Além disso, a análise qualitativa avalia os mecanismos físico-químicos e cinéticos subjacentes a essas rotas verdes, demonstrando como os métodos alternativos de síntese operam como estratégias eficientes de engenharia de cristais. Adicionalmente, materiais à base de HAp têm sido cada vez mais aplicados em contextos biomédicos e ambientais, incluindo engenharia de tecido ósseo e remoção de poluentes. Apesar desses avanços, ainda persistem desafios relacionados à reprodutibilidade, padronização e escalabilidade dos métodos de síntese verde. De modo geral, este estudo fornece uma visão estruturada e integrativa do campo, identificando tendências-chave, lacunas de pesquisa e direções futuras para o desenvolvimento de materiais à base de HAp mais sustentáveis e de alto desempenho.

Palavras-chave: *Biomateriais; Engenharia de Tecidos Ósseos; Economia Circular; Materiais Nanoestruturados; Valorização de Resíduos.*

1 INTRODUCTION

The increasing demand for advanced biomaterials capable of promoting tissue regeneration has emerged as a major challenge in modern biomedical engineering, driven by the need to restore or replace damaged biological structures (Garimella *et al*., 2024; George *et al*., 2022). In this context, the development of biomaterials that combine high biological performance with sustainable and cost-effective synthesis routes has gained increasing attention, driven by environmental concerns and the demand for greater healthcare accessibility (Weerarathna *et al*., 2024; Mamidi; Otero, 2024; Filip *et al*., 2022). Among the biomaterials investigated for these applications, hydroxyapatite (HAp), a calcium phosphate ceramic with the chemical formula $Ca_{10}(PO_4)_6(OH)_2$, stands out due to its close chemical similarity to the mineral phase of human bone and teeth (Ielo *et al*., 2022). This compositional similarity provides HAp with excellent biocompatibility, bioactivity, and osteoconductive properties, making it highly suitable for bone-related applications (Kim *et al*., 2022). As a result, HAp has been widely explored in bone tissue engineering, implant coatings, and drug delivery systems (Torres; Sousa; Cipreste, 2022). Consequently, significant research efforts have been directed toward optimizing synthesis methods and tailoring the physicochemical properties of HAp for improved performance (Souza *et al*., 2024).

Traditionally, HAp has been synthesized using conventional chemical routes such as precipitation, sol-gel, and hydrothermal methods, which allow precise control over particle size, morphology, and crystallinity (Wu *et al*., 2023). Despite their effectiveness, these methods often involve high energy consumption, elevated processing temperatures, and the use of potentially hazardous chemical

reagents (Noviyanti *et al*., 2022). Such limitations raise concerns regarding the environmental sustainability and large-scale applicability of conventional synthesis techniques (Abdulhussein *et al*., 2025). Within this framework, the use of biogenic and waste-derived precursors has gained increasing attention as a sustainable strategy for HAp production (Swarup *et al*., 2025). These strategies are aligned with the principles of green chemistry and circular economy, reinforcing their relevance in sustainable material design (Gün; Gurbanov; Tunali, 2025). Calcium-rich waste materials such as eggshells, seashells, and fish bones can be effectively converted into HAp, providing a low-cost and renewable source of raw materials (Muthu *et al*., 2022). Furthermore, this convergence between sustainable material design and waste valorization is directly aligned with the United Nations 2030 Agenda for Sustainable Development, particularly with Sustainable Development Goals (SDGs) 3 (Good Health and Well-Being), 6 (Clean Water and Sanitation), 9 (Industry, Innovation and Infrastructure), and 12 (Responsible Consumption and Production) (United Nations, 2015). The dual contribution of HAp-based materials to both biomedical and environmental challenges thus positions green synthesis as a strategic priority within global sustainability frameworks.

Beyond their environmental advantages, these biogenic precursors can significantly influence the structural, morphological, and biological properties of the resulting HAp due to their intrinsic chemical composition and the presence of trace elements (Brazdis *et al*., 2021). This aspect introduces an additional level of complexity and potential functionality, positioning waste-derived synthesis routes not only as sustainable alternatives but also as promising strategies for tailoring material performance (Prakash *et al*., 2024). However, despite these advances, significant challenges remain regarding the reproducibility of synthesis protocols, variability in precursor composition, and the lack of standardized methodologies across studies. Despite the increasing research interest in the green synthesis of HAp, the scientific literature remains fragmented, with many studies focusing on isolated synthesis methods or specific precursor sources (Kalbarczyk *et al*., 2022). This fragmentation hinders the identification of overarching research patterns, limits the comparative evaluation of different synthesis strategies, and restricts the recognition of emerging scientific trends (Wan; Cui; Wang, 2024). In this context, bibliometric approaches have emerged as powerful tools for systematically evaluating the evolution of scientific fields, enabling the analysis of publication trends, collaboration networks, and thematic structures (Ohemeng; Ramabodu, 2025).

Therefore, the present study aims to perform a comprehensive bibliometric analysis of scientific publications related to the green synthesis of HAp using biogenic and waste-derived precursors. Specifically, the study examines the temporal evolution of scientific production, the geographical distribution of research activity, the most frequent keywords, and the conceptual structure of the field through co-occurrence network analysis. In addition, the most influential publications were qualitatively analyzed to identify dominant synthesis routes, precursor types, and application trends. By providing a structured, critical, and integrative overview of the literature, this work not only

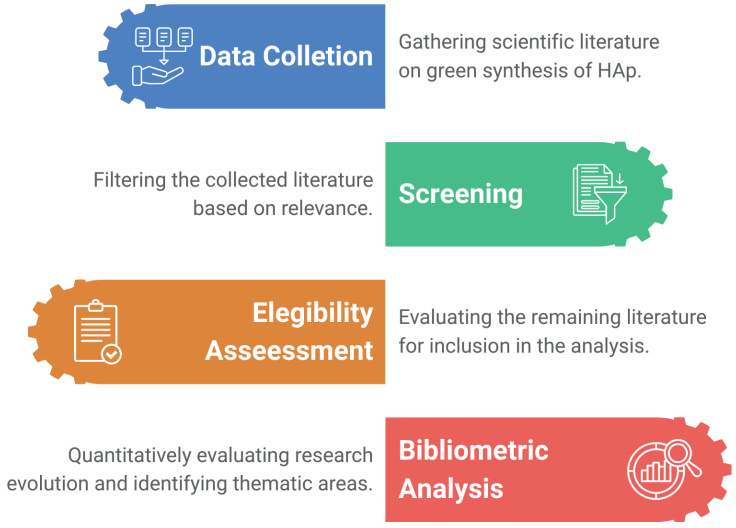
identifies existing research gaps but also supports the development of scalable, reproducible, and industrially viable green synthesis strategies for HAp production.

2 MATERIALS AND METHODS

2.1 STUDY DESIGN

This study employed a bibliometric approach to systematically analyze the scientific literature on the green synthesis of HAp derived from biogenic and waste-based precursors. This methodology was selected due to its ability to quantitatively evaluate the evolution of research, identify emerging thematic areas, assess global scientific contributions, and reveal the intellectual structure of the field over a defined time period (Donthu *et al.*, 2021). Furthermore, bibliometric analysis provides a reproducible and structured framework for examining publication patterns, knowledge development, and thematic consolidation, enabling a comprehensive understanding of the current research landscape (Öztürk; Kocaman; Kanbach, 2024). The methodological workflow adopted in this study consisted of four main stages, as illustrated in Figure 1.

Figure 1 - Methodological workflow of the study.



Source: Prepared by the author.

2.2 DATA SOURCE AND SEARCH STRATEGY

The dataset analyzed in this study was exclusively retrieved from the Scopus database, which was selected due to its extensive coverage of peer-reviewed literature, standardized metadata structure, and broad international indexing (Guerrero-Bote *et al.*, 2021). Data collection was conducted using the advanced search interface available in Scopus, applying a structured Boolean query designed to identify publications focused on environmentally sustainable synthesis routes for HAp, particularly

those involving natural or waste-derived calcium sources (Ng *et al.*, 2022). The search expression was defined as follows:

TITLE-ABS-KEY (("hydroxyapatite" OR "HAp" OR "calcium hydroxyapatite") AND ("green synthesis" OR "sustainable synthesis" OR "eco-friendly synthesis" OR "green route") AND ("biowaste" OR "waste-derived" OR "biogenic" OR "natural precursor" OR "eggshell" OR "sea-shell" OR "shell waste" OR "fish bone" OR "animal bone" OR "bovine bone" OR "calcium waste"))

To ensure specificity, descriptors related to hydroxyapatite and sustainable synthesis strategies were restricted to the title, abstract, and keyword fields. In contrast, terms associated with precursor sources were included to expand retrieval coverage and account for variations in terminology across studies. This search strategy was designed to achieve a balance between comprehensiveness and relevance, ensuring the identification of studies aligned with the objectives of this work.

2.3 INCLUSION AND EXCLUSION CRITERIA

Predefined eligibility criteria were established to ensure methodological consistency and reliability in the selection of publications. Only original research articles published in peer-reviewed journals, written in English, and available in their final version were included in the analysis. The temporal scope was restricted to publications from 2021 to 2025 in order to capture recent advances in sustainable hydroxyapatite synthesis and the use of alternative raw materials (Veluswamy *et al.*, 2024). This time frame allows for a focused assessment of current developments in the field.

Publications classified as review articles, conference proceedings, book chapters, editorials, and other non-primary research formats were excluded to avoid duplication of information and to maintain consistency in bibliometric indicators. After data export, duplicate records were removed. Subsequently, titles and abstracts were screened to verify alignment with the research scope. Only studies explicitly addressing the synthesis of hydroxyapatite through environmentally friendly methods using biogenic or waste-derived precursors were retained. Articles that did not clearly meet these criteria were excluded from the final dataset.

2.4 DATA EXTRACTION AND BIBLIOMETRIC ANALYSIS

All selected records were exported from the Scopus database in the BibTeX format to preserve complete bibliographic metadata, including authorship, institutional affiliations, titles, abstracts, keywords, publication year, journal sources, and citation data. The dataset was then processed using the Bibliometrix package within the RStudio environment (version 4.5.2), which enabled both descriptive

bibliometric analysis and science mapping (R Core Team, 2025; Aria; Cuccurullo, 2017). Initially, the temporal evolution of scientific production was analyzed to identify publication trends over the selected period. The geographical distribution of publications was also evaluated based on authors' affiliations, allowing the identification of the most active countries in the field.

Keyword analysis was performed to determine the most frequently occurring terms and to characterize the main research themes. In addition, a keyword co-occurrence network was constructed to explore conceptual relationships and identify major research clusters related to synthesis methods, precursor types, and application areas. A citation analysis was subsequently conducted to identify the most influential publications within the dataset. These studies were qualitatively examined to characterize predominant synthesis strategies, types of raw materials employed, and key properties of the synthesized hydroxyapatite.

Furthermore, the selected articles were manually categorized according to the origin of the precursor material, including groups such as eggshell-derived, seashell-derived, fish bone-derived, and other biogenic sources. This classification enabled a comparative analysis of research trends associated with different raw materials. Finally, graphical outputs and visual representations were refined using Python-based tools (version 3.12) to improve clarity, consistency, and overall presentation quality of the bibliometric results.

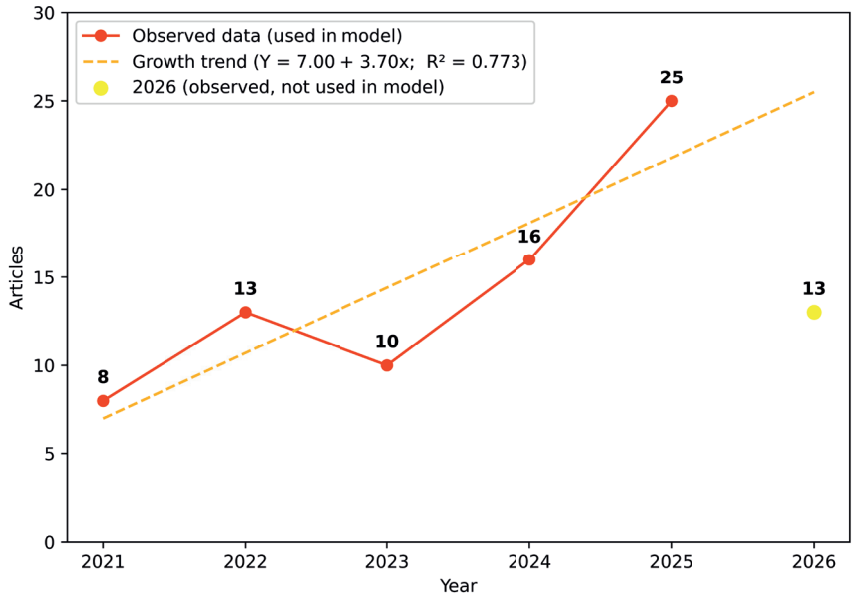
3 RESULTS AND DISCUSSION

The automated search in the Scopus database retrieved a dataset covering the period from 2021 to 2026. Following refinement and the application of inclusion and exclusion criteria for quantitative mapping, this process yielded a total of 85 original articles for the analyses of this study.

3.1 SCIENTIFIC PRODUCTION OVER TIME

The temporal distribution of publications revealed a progressive increase in the number of studies related to the green synthesis of hydroxyapatite using biogenic and waste-derived precursors over the analyzed period. As illustrated in Figure 2, a total of 8 articles were published in 2021, followed by a notable increase to 13 publications in 2022.

Figure 2 - Article production over time by Scopus database.



Source: Prepared by the author.

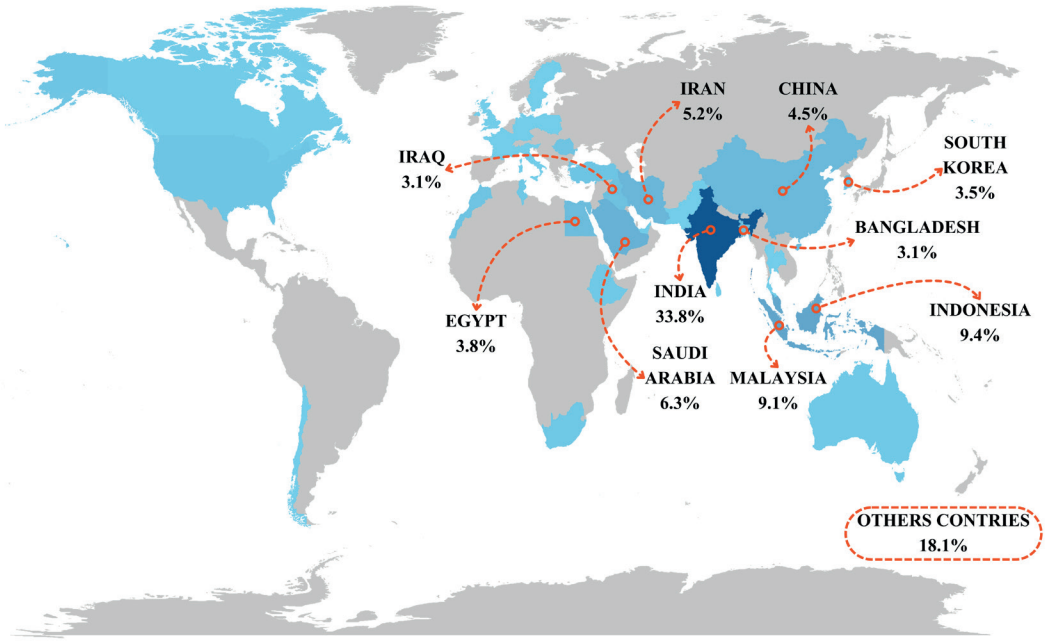
This initial growth suggests an early consolidation of interest in sustainable synthesis approaches within the research community. However, in 2023, a slight decline was observed, with the number of publications decreasing to 10. This temporary reduction may reflect a delayed impact of the COVID-19 pandemic. The laboratory closures and supply chain disruptions during 2020-2021 severely hindered practical experiments. Given the typical timeline for research execution and the peer-review pipeline, these operational constraints directly manifested as a drop in documented outputs by 2023 (Sohrabi *et al*., 2021). Despite this temporary reduction, the overall trend remains upward. From 2024 onwards, a consistent growth pattern was evident. The number of publications increased to 16 in 2024 and reached its peak at 25 articles in 2025. This significant rise indicates an intensification of research efforts, likely driven by increasing environmental concerns, the valorization of bio-waste materials, and the expanding application of hydroxyapatite in biomedical fields.

The linear regression model applied to the observed data demonstrates a positive growth trend, described by the equation $y = 7.00 + 3.70x$, with a coefficient of determination (R^2) of 0.773. This value indicates a strong correlation between publication year and the number of articles, suggesting a consistent expansion of the research field over time. Although the value for 2026 (13 publications) was not included in the regression model, it appears lower than expected when compared to the projected trend line. This discrepancy is likely due to the incomplete nature of the current year, as not all studies have been indexed or published at the time of data collection. Overall, the results indicate that research on green synthesis routes for HAp-derived from alternative natural sources is experiencing sustained growth, reflecting its increasing relevance in the context of sustainable materials science and biomedical engineering.

3.2 GEOGRAPHIC DISTRIBUTION OF SCIENTIFIC PRODUCTION

The geographical distribution of scientific production reveals a strong concentration of research activity in specific regions, with a clear predominance of Asian countries in the field of green synthesis of hydroxyapatite. A total of 287 authors were identified across the selected articles (N=85). The geographic distribution of these authors is illustrated in Figure 3.

Figure 3 - Geographical distribution for the authors across the obtained publications in the Scopus database.



Source: Prepared by the author.

India emerges as the leading contributor, accounting for 33.8% of the total publications, with 97 authors. This substantial dominance indicates a highly consolidated research effort, likely driven by the availability of biogenic raw materials, strong academic interest in sustainable technologies, and the growing demand for low-cost biomaterials. Following India, Indonesia and Malaysia represent the second tier of productivity, contributing 9.4% (27 authors) and 9.1% (26 authors), respectively. These countries also demonstrate a significant engagement in sustainable material research, particularly due to the abundance of natural waste resources such as seashells and agricultural by-products.

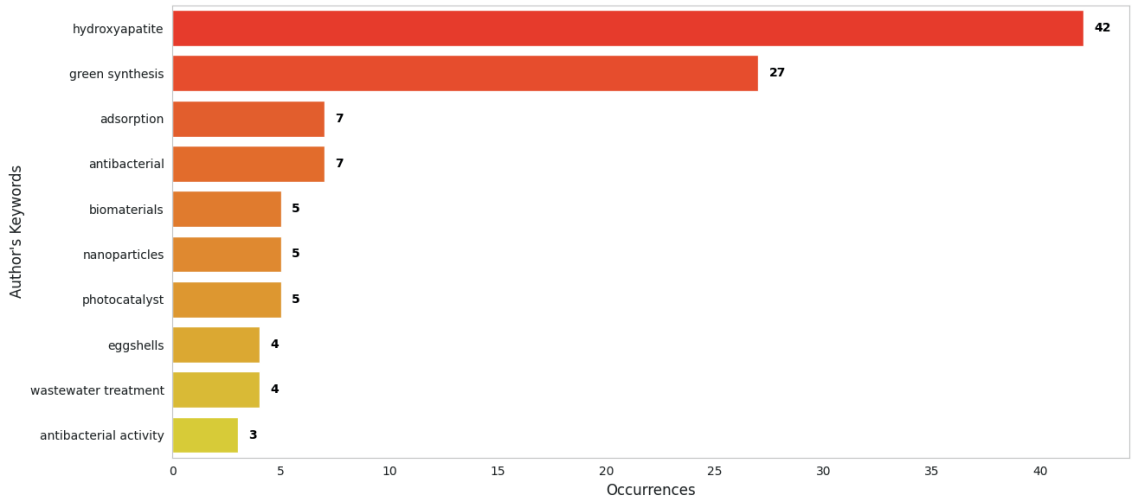
Saudi Arabia (6.3%) and Iran (5.2%) further contribute to the development of this research field, reflecting increasing investments in advanced materials and environmental sustainability. China, despite its global prominence in materials science, appears with a relatively moderate contribution (4.5%), which may indicate a broader diversification of research topics rather than a specific focus on green hydroxyapatite synthesis. Other countries, including Egypt (3.8%), South Korea (3.5%), Bangladesh (3.1%), and Iraq (3.1%), present smaller yet relevant contributions, highlighting the global expansion of interest in sustainable synthesis routes.

The "Others" category accounts for 18.1% of the countries, indicating a wide dispersion of research efforts across multiple countries with lower individual outputs. This suggests that, although the field is led by a few dominant nations, it is progressively gaining international attention. Overall, the results demonstrate that research on green synthesis of HAp is geographically concentrated but steadily expanding worldwide. The strong presence of developing and emerging economies reinforces the relevance of this topic in regions where low-cost, sustainable, and waste-derived materials are particularly valuable for technological and biomedical applications.

3.3 KEYWORD ANALYSIS AND RESEARCH TRENDS

The analysis of author's keywords provides important insights into the main research directions and thematic structure of the field. As shown in Figure 5, the most frequently occurring keyword is hydroxyapatite, with 42 occurrences, confirming its central role as the primary material investigated in the selected studies.

Figure 4 - Most frequent keywords identified in the analyzed publications.



Source: Prepared by the author.

The term green synthesis is prominently featured as the second most frequent keyword, with 27 occurrences. This strong representation highlights a significant research emphasis on environmentally sustainable and eco-friendly production methods, reinforcing the growing integration of green chemistry principles in the synthesis of hydroxyapatite-based materials. In addition to these foundational concepts, several keywords related to potential applications and properties are well represented. The terms adsorption (7 occurrences) and wastewater treatment (4 occurrences) collectively indicate that hydroxyapatite synthesized via green routes is being actively explored for environmental applications, particularly in pollutant removal and water purification. Concurrently, the material's biomedical relevance is underscored by the keywords antibacterial (7 occurrences) and antibacterial activity

(3 occurrences), demonstrating a clear interest in evaluating its functional biological properties for medical or antimicrobial applications.

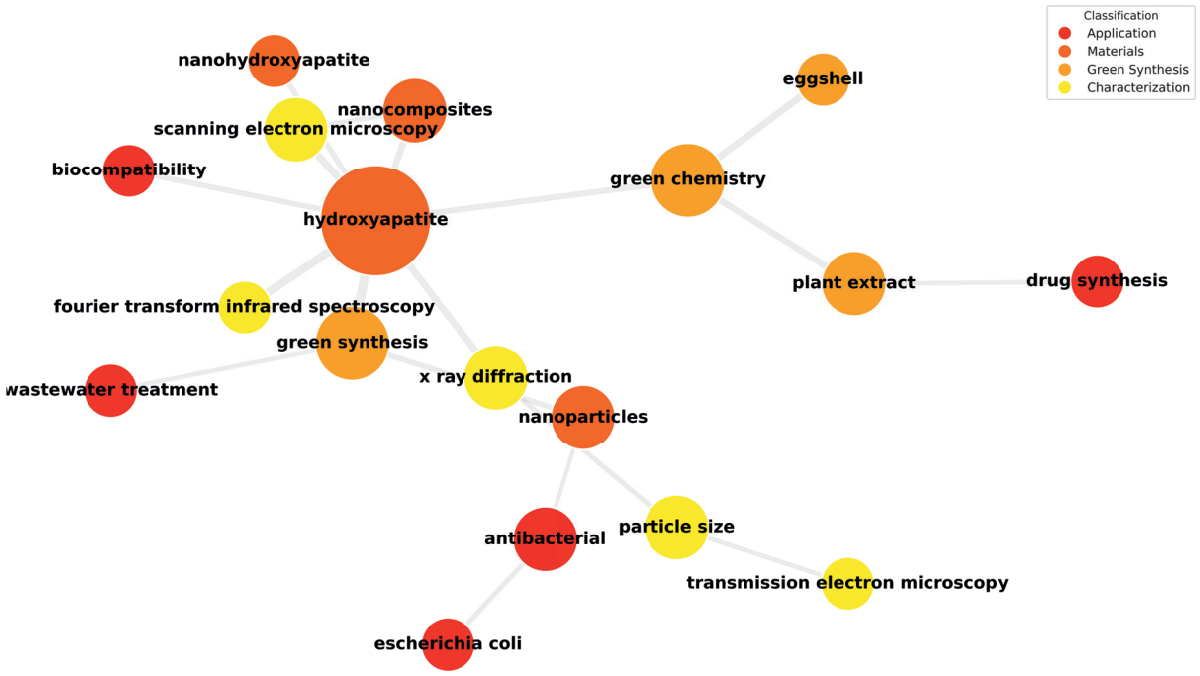
The presence of terms such as nanoparticles (5 occurrences) and photocatalyst (5 occurrences) suggests that a substantial portion of the studies focuses on nanotechnology and advanced functional materials, where nanoscale control is crucial to enhancing catalytic or structural performance. Furthermore, the keyword eggshells (4 occurrences) is highly noteworthy, as it specifies a prominent alternative and biogenic waste source utilized for extracting or synthesizing calcium-rich hydroxyapatite, aligning perfectly with circular economy principles. The term biomaterials (5 occurrences) further solidifies the multidisciplinary nature of this field, linking material science directly to tissue engineering or bone-related applications.

Overall, the keyword analysis reveals that the research field is structured around three main pillars: (i) sustainable synthesis approaches and waste valorization, as highlighted by green synthesis and the use of eggshells, (ii) material properties and scale, represented by nanoparticles and antibacterial activity, and (iii) application-oriented studies, spanning both the biomedical field with biomaterials and environmental remediation through adsorption and wastewater treatment. This distribution indicates a dynamic and multidisciplinary research area, with increasing integration between green chemistry principles and functional material development.

3.4 KEYWORD CO-OCCURRENCE NETWORK AND THEMATIC CLUSTERS

The keyword co-occurrence network reveals the conceptual organization of the research field, allowing the identification of distinct thematic clusters based on the strength of relationships between terms. As shown in Figure 5, the network is divided into four main clusters, each representing a specific research direction within the green synthesis of hydroxyapatite.

Figure 5 - Expanded co-occurrence network of keywords identified in the analyzed publications.



Source: Prepared by the author.

Cluster 1 (red - Application) is primarily associated with the application of HAp-based materials. This cluster includes keywords such as biocompatibility, antibacterial, *Escherichia coli*, wastewater treatment, and drug synthesis. The presence of these terms indicates that a significant portion of the research is directed toward biomedical and environmental applications. In particular, the strong linkage between antibacterial and *Escherichia coli* highlights the frequent use of microbial models to evaluate antimicrobial properties. Additionally, wastewater treatment suggests the growing interest in HAp as an adsorbent material for environmental remediation.

Cluster 2 (orange - Materials) represents the core material development domain and is centered around HAp, the most connected node in the network. This cluster also includes terms such as nanocomposites, nanoparticles, and nanohydroxyapatite, indicating a strong emphasis on nanoscale engineering and material optimization. The connections within this cluster suggest that research efforts are focused on improving structural, mechanical, and functional properties of HAp through the development of advanced material systems.

Cluster 3 (yellow - Characterization) encompasses the main analytical techniques used to evaluate synthesized materials. Keywords such as X-ray diffraction, scanning electron microscopy, transmission electron microscopy, Fourier transform infrared spectroscopy, and particle size are included in this group. The prominence of this cluster demonstrates the critical role of physicochemical characterization in confirming phase composition, morphology, and structural integrity of HAp produced via green routes.

Cluster 4 (light orange - Green Synthesis) is associated with environmentally friendly synthesis approaches and the use of alternative precursors. This cluster includes terms such as green synthesis, green chemistry, plant extract, and eggshell. The connections observed within this cluster highlight the increasing adoption of sustainable methodologies, particularly those involving biological agents and calcium-rich waste materials. The link between plant extract and green chemistry suggests the growing relevance of bio-mediated synthesis processes.

Overall, the network structure indicates a well-defined and interconnected research field, where sustainable synthesis methods (Cluster 4) are directly linked to material development (Cluster 2), supported by rigorous characterization techniques (Cluster 3), and ultimately directed toward practical applications (Cluster 1). This integrated framework reflects the multidisciplinary nature of current research and suggests a continuous trend toward the development of functional, sustainable, and application-oriented HAp-based materials.

3.5 BIBLIOMETRIC ANALYSIS AND LEADING CONTRIBUTIONS

The integration of bibliometric indicators with qualitative analysis provides a comprehensive understanding of the evolution and current structure of research on the green synthesis of HAp derived from biogenic and waste-based precursors. In this view, Table 1 highlights the most influential studies from the obtained dataset.

TABLE 1 - Main articles identified in the Scopus database.

AUTHOR/ YEAR	TITLE	JOURNAL	DOI	N° CITATIONS
VINAYAGAM, R. (2023)	Bioinspiration synthesis of hydroxyapatite nanoparticles using eggshells as a calcium source: Evaluation of Congo red dye adsorption potential	Journal of Materials Research and Technology	10.1016/j.jmrt.2022.11.093	91
VINAYAGAM, R. (2022)	Green synthesized hydroxyapatite nanoadsorbent for the adsorptive removal of AB113 dye for environmental applications	Environmental Research	10.1016/j.envres.2022.113274	67
OBAYOMI, K. (2023)	Green synthesis of graphene-oxide based nanocomposites for efficient removal of methylene blue dye from wastewater	Desalination	10.1016/j.desal.2023.116749	67
ALI, A. (2021)	Novel green synthesis of hydroxyapatite uniform nanorods via microwave-hydrothermal route using licorice root extract as template	Ceramics International	10.1016/j.ceramint.2020.09.256	66
SIN, J. (2021)	*Punica granatum* mediated green synthesis of cauliflower-like ZnO and decorated with bovine bone-derived hydroxyapatite for expeditious visible light photocatalytic antibacterial, antibiofilm and antioxidant activities	Journal of Environmental Chemical Engineering	10.1016/j.jece.2021.105736	63

SULTANA, S. (2021)	UV-assisted synthesis of hydroxyapatite from eggshells at ambient temperature: cytotoxicity, drug delivery and bioactivity	RSC Advances	10.1039/d0ra09673c	60
SODHANI, H. (2022)	Adsorptive removal of Acid Blue 113 using hydroxyapatite nanoadsorbents synthesized using *Peltophorum pterocarpum* pod extract	Chemosphere	10.1016/j.chemosphere.2022.134752	55
SHALTOUT, W. (2024)	Synthesis and characterization of ferric@ nanocellulose/nanohydroxyapatite bio-composite based on sea scallop shells and cotton stalks: adsorption of Safranin-O dye	Biomass Conversion and Biorefinery	10.1007/s13399-022-02753-1	53
SURESH, R. (2021)	Recent progress in green and biopolymer based photocatalysts for the abatement of aquatic pollutants	Environmental Research	10.1016/j.envres.2021.111324	45
GHATE, P. (2022)	Synthesis of hydroxyapatite nanoparticles using Acacia falcata leaf extract and study of their anticancerous activity against cancerous mammalian cell lines	Environmental Research	10.1016/j.envres.2022.113917	44

Source: Prepared by the author.

The temporal distribution of publications reveals a clear upward trend, particularly after 2023, indicating the progressive consolidation of sustainable synthesis strategies within the field. This growth is strongly aligned with global efforts toward circular economy practices and the increasing demand for low-cost biomaterials obtained from renewable or waste-derived sources. In parallel, the geographical distribution highlights a strong concentration of research output in emerging economies, particularly in Asia, where countries such as India, Indonesia, and Malaysia dominate scientific production. This pattern can be directly associated with the availability of calcium-rich residues and the strategic prioritization of sustainable technologies in these regions.

From a conceptual standpoint, the structure of the field is organized around four interconnected domains: (*i*) green synthesis methodologies, (*ii*) material design and optimization, (*iii*) physicochemical characterization, and (*iv*) application-driven research. Within this framework, hydroxyapatite acts as a central platform material, linking environmentally friendly synthesis strategies to functional performance across biomedical and environmental applications. A deeper examination of the most cited publications reveals three major scientific directions that currently define the field.

The first direction is centered on bio-mediated and waste-derived synthesis strategies, where natural extracts and biogenic precursors are employed not only as raw materials but also as functional agents in the synthesis process. Studies by Vinayagam *et al.* (2022; 2023) exemplify this approach by demonstrating the use of plant-derived extracts and waste materials such as eggshells to control nucleation and crystal growth, resulting in hydroxyapatite with improved crystallinity and tailored morphology. These findings highlight the dual role of phytochemicals as both reducing and structure-directing agents, reinforcing the potential of fully green synthesis routes.

The second direction involves the development of hybrid and multifunctional material systems, in which hydroxyapatite is combined with additional phases to enhance its functional properties.

The work of Obayomi *et al.* (2023) illustrates this trend through the integration of multiple waste-derived precursors with graphene oxide and bioactive organic components, resulting in composite systems with improved structural and functional performance. Similarly, Shaltout *et al.* (2024) extend this concept by incorporating nanocellulose derived from agricultural residues into nanohydroxyapatite-based biocomposites, demonstrating a clear shift toward structurally complex and multifunctional materials. These approaches indicate that the field is evolving beyond single-phase materials toward engineered composites with synergistic properties.

The third direction is associated with the expansion of application domains, particularly in environmental and biomedical contexts. Environmental applications are strongly represented by studies such as those of Sin *et al.* (2021) and Sodhani *et al.* (2022), which demonstrate the effectiveness of HAp-based materials in adsorption and antimicrobial processes. The incorporation of secondary phases, such as ZnO in the study by Sin *et al.* (2021), significantly enhances antibacterial performance, while the high surface area nanostructures reported by Sodhani *et al.* (2022) improve adsorption efficiency. In parallel, Ghate *et al.* (2022) highlight the potential of biogenically synthesized HAp nanoparticles in biomedical applications beyond bone regeneration, including anticancer activity, reinforcing the versatility of the material.

Within the biomedical domain, particularly in bone tissue engineering, studies by Sultana *et al.* (2021) and Ali *et al.* (2021) demonstrate a clear transition toward low-energy and morphology-controlled synthesis routes. Sultana *et al.* (2021) propose a UV-assisted solid-state synthesis using eggshell-derived precursors, achieving high bioactivity with minimal energy input. In contrast, Ali *et al.* (2021) employ a microwave-assisted hydrothermal method combined with plant extracts to produce nanorod-shaped hydroxyapatite with enhanced surface properties, favorable for cell adhesion and proliferation. These studies highlight the importance of controlling synthesis conditions to tailor biological performance. In addition to experimental advancements, the work of Suresh *et al.* (2021) provides a broader conceptual perspective by positioning HAp as a key inorganic component within green and biopolymer-based material systems. This contribution reinforces the theoretical foundation of the field and supports the integration of hydroxyapatite into multifunctional and sustainable biomaterial platforms.

Overall, the combined analysis of bibliometric trends and leading contributions indicates that the field is undergoing a transition from conventional synthesis approaches toward more sustainable, multifunctional, and application-oriented strategies. The convergence of waste valorization, biomediated synthesis, and advanced material design reflects a shift toward the development of high-performance systems tailored for specific biomedical and environmental applications. These findings suggest that future research will likely focus on the optimization of hybrid materials, the development of low-energy synthesis methods, and the expansion of hydroxyapatite-based systems in advanced applications, particularly in bone tissue engineering.

3.6 PRINCIPAL FINDINGS AND TRENDS

The integrated evaluation of the most cited studies, supported by bibliometric indicators and DOI-based analysis, reveals a set of converging findings that define the current evolution of green HAp synthesis using biogenic and waste-derived precursors. One of the most prominent trends is the consolidation of circular economy principles as a central paradigm in the field. The consistent use of calcium-rich residues (such as eggshells, fish bones, and marine shells) demonstrates a clear shift from conventional raw materials toward waste valorization strategies. This transition not only reduces production costs but also aligns hydroxyapatite synthesis with global sustainability goals, reinforcing its role within environmentally responsible material design frameworks. Moreover, the integration of multiple waste streams, including agricultural and marine residues, indicates a movement toward more holistic and resource-efficient production systems.

Another significant development is the transition toward low-energy and environmentally benign synthesis routes. Conventional high-temperature and chemically intensive processes are increasingly being replaced by alternative methods operating under mild conditions, including microwave-assisted, UV-assisted, and modified hydrothermal techniques. These approaches contribute to reduced energy consumption, shorter processing times, and improved scalability, suggesting that the field is progressing toward industrially viable green synthesis pathways. The growing incorporation of natural organic agents and plant-derived extracts represents an additional key advancement. These compounds act as multifunctional components during synthesis, serving as reducing agents, stabilizers, and structure-directing templates. This substitution of synthetic additives not only minimizes the use of hazardous chemicals but also enhances the biocompatibility and environmental safety of the resulting materials. Furthermore, the presence of bioactive molecules may contribute to improved biological interactions, particularly in biomedical applications.

A parallel trend is the increasing emphasis on nanostructuring and morphological control, which has become a critical factor in tailoring material performance. The formation of well-defined nanostructures (such as nanorods, needle-like particles, and polycrystalline assemblies) demonstrates the ability to precisely manipulate crystal growth through green synthesis routes. These morphological features are particularly relevant for applications requiring high surface area and enhanced interfacial interactions, such as bone tissue engineering and adsorption processes. In addition, the field is undergoing a clear transition toward the development of hybrid and multifunctional material systems. The incorporation of secondary phases, including graphene-based materials, metal oxides, and biopolymers, has enabled the design of composites with enhanced mechanical, antibacterial, and adsorption properties. This shift reflects a broader movement from single-phase HAp toward engineered systems with synergistic functionalities, expanding the material's applicability across multiple domains.

The diversification of application areas further reinforces this trend. While hydroxyapatite remains strongly associated with biomedical applications - particularly in bone regeneration and tissue engineering - there is a growing expansion into environmental and interdisciplinary fields. Applications such as pollutant removal, antimicrobial systems, and anticancer platforms demonstrate the versatility of HAp as a multifunctional material, capable of addressing challenges beyond its traditional biomedical scope. Finally, the analyzed studies collectively support a conceptual transition in which HAp is no longer viewed solely as a bioactive ceramic, but rather as a platform material within sustainable and multifunctional systems. This perspective emphasizes the integration of green chemistry principles, material design, and application-oriented performance, positioning HAp at the intersection of biomaterials science and environmental engineering.

Overall, the findings indicate that the field is evolving toward a convergence of sustainability, structural control, and functional integration. The green synthesis of HAp has progressed beyond environmentally friendly production, emerging as a strategic approach for the development of advanced materials tailored to complex biomedical and environmental applications. Future research is expected to further explore hybrid systems, optimize low-energy synthesis routes, and expand the functional scope of HAp-based materials.

3.7 MECHANISMS IN GREEN ROUTES

To overcome the descriptive nature of bibliometric data, understanding the physicochemical mechanisms governing green HAp routes is essential. Using biogenic waste and plant extracts introduces biomolecules (such as polyphenols and saponins) that act as chelating agents and structure-directing templates. These molecules coordinate with free calcium ions, reducing the free energy required for nucleation and controlling oriented crystal growth, typically along the c-axis. Table 2 presents a compact summary of these precursors, properties, and the exact mechanisms dictating green HAp functionality.

Table 2 - Streamlined summary of chemical mechanisms and properties of green HAp.

AUTHOR/ YEAR	GREEN SOURCE AND METHOD	PROPERTIES AND APPLICATION	PREDOMINANT PHYSICOCHEMICAL MECHANISM
VINAYAGAM, R. (2023)	Eggshells / Natural extract	High surface area spheres / Congo Red adsorption	Chemisorption and Electrostatics: Coulombic attraction between anionic sulfonate groups of the dye and protonated calcium sites on the HAp surface.
VINAYAGAM, R. (2022)	Eggshells / Phyto-chemical route	Crystalline nano--adsorbent / Acid Blue 113 removal	Ion Exchange and Hydrogen Bonding: Surface interaction with dye amines and anion exchange with lattice phosphate groups.
OBAYOMI, K. (2023)	Integrated waste / Graphene oxide	Porous nanocomposite / Methylene Blue removal	Synergistic Pi-Pi and Electrostatics: Pi-pi stacking between dye aromatic rings and graphene oxide, with strong anchoring by phosphates and carboxyls.

ALI, A. (2021)	Standard source / Licorice + Microwave	Uniform nanorods / Bone tissue engineering	Capping Agent-Directed Growth: Saponins act as surfactants on lateral facets, forcing unidirectional crystallization along the c-axis.
SIN, J. (2021)	Bovine bone / Pomegranate + Zinc oxide	Cauliflower-like structure / Photocatalysis and Antibacterial	Semiconductor Heterojunction: HAp disperses zinc oxide while phytochemicals extend the lifetime of photogenerated electrons, producing free radicals.
SULTANA, S. (2021)	Eggshells / UV radiation	Stable nanoparticles / Drug delivery	Photo-assisted Nucleation: Ultraviolet radiation generates free radicals in precursors, enabling pure crystallization at room temperature.
SODHANI, H. (2022)	Converted source / Peltophorum pterocarpum	Porous nano-adsorbent / Acid Blue 113 removal	Inner-Sphere Coordination: Direct chemical complexation and chemisorption of the pollutant onto calcium-rich cleavage planes of HAp.
SHALTOUT, W. (2024)	Shells / Nanocellulose + Magnetite	Hybrid biocomposite / Safranin-O adsorption	Multicenter Complexation: Nanocellulose provides a flexible hydrophilic network, while biogenic HAp ensures fixed ion-exchange sites.
SURESH, R. (2021)	Natural matrices / Biopolymers	Integrated system / Pollutant degradation	Conductive Support: The HAp matrix immobilizes the active semiconductor and retains the pollutant near oxidative radical generation sites.
GHATE, P. (2022)	Biogenic source / Acacia falcata	Functionalized spheroids / Antitumor activity	Endocytosis and Apoptosis: Nanoparticles release excess calcium ions inside the acidic lysosomal environment of the tumor, triggering the mitochondrial pathway.

Source: Prepared by the author.

The consolidated analysis in Table 2 demonstrates that the green synthesis of HAp transcends simple reagent replacement; it operates as an efficient crystal engineering strategy. In pollutant removal, adsorptive efficiency is dictated by modulating surface charge density and the point of zero charge of the material. The presence of residual phytochemicals anchored to the crystal surface drives the process toward inner-sphere coordination chemisorption and selective electrostatic interactions, outperforming traditional synthetic adsorbents.

From a kinetic and thermodynamic perspective, alternative energy sources like microwaves and ultraviolet radiation drastically alter nucleation rates. While microwaves promote rapid volumetric heating that restricts radial growth to yield uniform nanorods, ultraviolet radiation overcomes thermal barriers by inducing excited electronic states, enabling synthesis at room temperature.

Additionally, the natural doping effect from biogenic precursors (such as eggshells and scallop shells) is highly significant, as they naturally contain traces of magnesium, strontium, and carbonate. The isomorphic substitution of these ions into the HAp lattice creates local distortions and structural vacancies. These imperfections increase the surface free energy of green HAp, enhancing both the dispersion of active catalytic phases and biological reactivity in tumor treatments under acidic pH gradients.

4 CONCLUSION

This study provided a comprehensive bibliometric and qualitative analysis of the scientific literature on the green synthesis of HAp using biogenic and waste-derived precursors, highlighting the main developments, research trends, and emerging directions in the field. The results demonstrated a consistent growth in scientific production in recent years, reflecting the increasing relevance of sustainable material design and the global transition toward circular economy practices. The predominance of research contributions from emerging economies further emphasized the strong connection between resource availability and the development of environmentally friendly synthesis strategies.

The combined analysis revealed that the field is structured around key interconnected domains, including green synthesis methodologies, material optimization, physicochemical characterization, and application-driven research. Within this framework, HAp has evolved from a conventional biomaterial to a versatile platform capable of integrating sustainability, functionality, and performance. The main findings indicated a clear shift toward the use of waste-derived raw materials, low-energy synthesis routes, and bio-mediated processes, which collectively contribute to reducing environmental impact while maintaining or enhancing material properties. In addition, the increasing development of hybrid and multifunctional systems demonstrated a transition toward more complex and application-oriented material designs. By bridging bibliometric trends with fundamental science, this work elucidates the exact physicochemical and thermodynamic mechanisms that govern green synthesis, moving beyond descriptive metrics to establish HAp as a highly tailored platform material.

Furthermore, the diversification of application areas (ranging from bone tissue engineering to environmental remediation and antimicrobial systems) highlighted the expanding role of HAp in addressing multidisciplinary challenges. These advances reinforced the potential of green synthesis strategies not only as sustainable alternatives but also as pathways for engineering high-performance materials. Despite these advances, the analysis also revealed gaps related to the standardization of synthesis protocols, scalability of green methods, and long-term performance evaluation, particularly in biomedical applications. Addressing these challenges will be essential for translating laboratory-scale developments into practical and industrial applications.

Overall, this study contributes to a deeper understanding of the current state of research and provides a structured overview that may guide future investigations. By systematizing these advances, this study also contributes to the consolidation of HAp-based green synthesis as a research field aligned with the 2030 Agenda for Sustainable Development. It is expected that upcoming studies will focus on optimizing hybrid systems, improving process efficiency, and expanding the functional scope of HAp-based materials, reinforcing their relevance within sustainable and advanced material science.

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