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SCIENTIFIC TRENDS IN 3D BIOPRINTING OF BIOACTIVE GLASS-ALGINATE COMPOSITES FOR BONE REGENERATION: A BIBLIOMETRIC STUDY

TENDÊNCIAS CIENTÍFICAS NA BIOIMPRESSÃO 3D DE COMPÓSITOS DE BIOVIDRO-ALGINATO PARA REGENERAÇÃO ÓSSEA: UM ESTUDO BIBLIOMÉTRICO

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ABSTRACT

The rapid development of additive manufacturing technologies has expanded the possibilities for designing advanced biomaterials for bone tissue repair. In this context, hydrogel-based systems reinforced with bioactive ceramics have attracted increasing attention due to their ability to combine structural support with biological functionality. This study presents a Scopus-based bibliometric analysis of scientific literature addressing composite biomaterials based on alginate and bioactive glass applied in 3D printing strategies for bone tissue engineering. Bibliographic records were retrieved from the Scopus database using a structured Boolean search strategy and filtered according to predefined eligibility criteria, resulting in a dataset of 98 peer-reviewed articles published between 2021 and 2026. The analysis examined the temporal evolution of scientific production, geographical distribution of publications, most frequent keywords, expanded keyword co-occurrence networks, and citation performance of the most influential studies. The results indicate a consistent growth in scientific output, reflecting the consolidation of this interdisciplinary research field. China and Iran emerged as the leading contributors to global scientific production, while other countries, including Portugal, South Korea, and Brazil, also demonstrated relevant participation in the research landscape. Citation analysis revealed that recent studies predominantly focus on hybrid material systems combining natural polymers with inorganic phases or functional nanomaterials to improve mechanical stability and biological performance. Overall, the findings highlight a transition toward multifunctional biomaterial platforms designed to enhance bone regeneration.

Keywords: Additive Manufacturing; Biomaterials; Hydrogel Scaffolds; Regenerative Medicine; Tissue Engineering.

RESUMO

O rápido desenvolvimento das tecnologias de manufatura aditiva ampliou as possibilidades para o desenvolvimento de biomateriais avançados destinados ao reparo do tecido ósseo. Nesse contexto, sistemas

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baseados em hidrogéis reforçados com cerâmicas bioativas têm atraído crescente atenção devido à sua capacidade de combinar suporte estrutural e funcionalidade biológica. Este estudo apresenta uma análise bibliométrica baseada na base de dados Scopus da literatura científica sobre biomateriais compósitos baseados em alginato e vidro bioativo aplicados em estratégias de impressão 3D para engenharia de tecido ósseo. Os registros bibliográficos foram recuperados da base de dados Scopus por meio de uma estratégia de busca Booleana estruturada e filtrados conforme critérios de elegibilidade previamente definidos, resultando em um conjunto de 98 artigos revisados por pares publicados entre 2021 e 2026. A análise avaliou a evolução temporal da produção científica, a distribuição geográfica das publicações, as palavras-chave mais frequentes, redes de coocorrência de palavras-chave e o desempenho de citação dos estudos mais influentes. Os resultados indicam crescimento consistente da produção científica, refletindo a consolidação desse campo interdisciplinar. China e Irã destacaram-se como os principais contribuintes para a produção científica global, enquanto países como Portugal, Coreia do Sul e Brasil também apresentaram participação relevante. A análise de citações mostrou que estudos recentes se concentram em sistemas híbridos que combinam polímeros naturais com fases inorgânicas ou nanomateriais funcionais para melhorar a estabilidade mecânica e o desempenho biológico. De modo geral, os resultados evidenciam uma transição para plataformas de biomateriais multifuncionais voltadas à regeneração óssea.

Palavras-chave: *Manufatura Aditiva; Biomateriais; Estruturas de Hidrogel; Medicina Regenerativa; Engenharia de Tecidos.*

1 INTRODUCTION

The increasing prevalence of bone defects caused by trauma, tumor resection, degenerative diseases, and congenital disorders represents a significant clinical challenge in modern healthcare (Zhu *et al*., 2023). Critical-sized bone defects exceed the intrinsic regenerative capacity of bone tissue and therefore require therapeutic intervention to restore both structural integrity and biological function (Zhou *et al*., 2025). Although autografts remain the clinical gold standard because of their osteoconductive and osteogenic properties, their application is limited by several drawbacks, including donor-site morbidity, restricted tissue availability, and the need for additional surgical procedures (Dalfino *et al*., 2023). For this reason, alternative strategies such as allografts and xenografts have been investigated. Nevertheless, these approaches are often associated with immunological complications and inconsistent long-term outcomes (Qi; Zhang; Lian, 2025). In response to these limitations, the development of advanced biomaterial-based solutions within the field of bone tissue engineering has received growing attention (Tang *et al*., 2025). This multidisciplinary field focuses on the design of scaffolds that mimic the structural, mechanical, and biochemical characteristics of native bone while simultaneously promoting cellular adhesion, proliferation, and osteogenic differentiation (Qin *et al*., 2025).

Among the biomaterials investigated for bone regeneration, bioactive glasses have attracted considerable attention because of their ability to chemically bond with bone tissue and stimulate osteogenesis through the controlled release of therapeutic ions (Shoushtari *et al*., 2024). When exposed to physiological environments, these materials undergo a sequence of surface reactions that culminate in the formation of a hydroxycarbonate apatite layer similar to the mineral phase of bone, thereby promoting strong interfacial integration with the host tissue (Li *et al*., 2021). Moreover, the release of biologically active ions such as silicon and calcium has been shown to enhance cellular signaling processes and to support osteogenic differentiation pathways (Maximov *et al*., 2021). In addition to these biological effects, the compositional flexibility of bioactive glasses enables precise modulation of degradation behavior and biological performance (Zhao *et al*., 2022). As a result, this tunability further broadens their potential for applications in bone tissue regeneration.

Naturally derived polymers have been extensively investigated as scaffold matrices owing to their inherent biocompatibility and ease of processing (Zhu *et al*., 2021). Among these materials, sodium alginate has become one of the most widely used hydrogel systems due to its mild ionic crosslinking mechanism, high water retention capacity, and structural similarity to the extracellular matrix (Ferjaoui *et al*., 2024). Together, these attributes favor efficient cell encapsulation while simultaneously enabling adequate nutrient and metabolite diffusion within three-dimensional constructs (Sadeghianmaryan *et al*., 2022). Despite these advantages, alginate-based hydrogels present limited mechanical strength and do not exhibit intrinsic osteoinductive activity, which constrains their application in load bearing bone regeneration (Cao *et al*., 2025). Consequently, composite strategies incorporating bioactive glass particles into alginate matrices have been increasingly proposed (Guagnini *et al*., 2024; Mostajeran; Baheiraei; Bagheri, 2024). In such systems, the cytocompatibility and printability of hydrogels are combined with the mechanical reinforcement and bioactivity provided by the inorganic phase (Mohammadzadeh *et al*., 2025). Therefore, these hybrid formulations support the development of multifunctional bioinks capable of maintaining structural fidelity while promoting controlled ionic release and enhanced osteogenic potential (Yao *et al*., 2022).

Simultaneously, the emergence of three-dimensional (3D) bioprinting technologies has substantially transformed the field of bone tissue engineering (Dukle *et al*., 2022). These approaches enable the precise spatial deposition of biomaterials and living cells within predefined architectures, thereby facilitating the fabrication of complex and biomimetic constructs (Flores-Torres *et al*., 2023). Among the available techniques, extrusion-based bioprinting has proven particularly suitable for hydrogel-based systems, as it allows accurate control over pore geometry, filament orientation, and overall scaffold architecture (Krishna; Sankar, 2024). Such parameters are critical for ensuring adequate mechanical stability, efficient mass transport, and proper tissue integration (Ender *et al*., 2021). Consequently, the combination of bioactive glass-alginate composite systems with 3D bioprinting technologies has emerged as a promising strategy for the development of advanced constructs designed for bone regeneration (Tu *et al*., 2023; Guo *et al*., 2024). Despite the rapid growth of research at the intersection of bioactive glass, alginate hydrogels, and 3D bioprinting, the scientific literature remains dispersed across several disciplines, including materials science, biofabrication, and regenerative medicine (Tahmasebifar *et al*., 2024). Furthermore, the significant variability in material formulations, printing parameters, and biological evaluation methodologies complicates cross-study comparisons and limits the identification of consolidated research directions and emerging scientific trends (Liu *et al*., 2025).

Although several general reviews have addressed the broad field of 3D bioprinting, hydrogel-based bioinks, and bone tissue engineering, these studies are predominantly narrative and lack quantitative assessments focused on the synergy between sodium alginate and bioactive glasses (Wei *et al*., 2023). This material combination has emerged as a key milestone in bone tissue engineering due to its dual-functional profile, with alginate providing controllable shear-thinning printability and mild ionic crosslinking, while bioactive glass contributes osteoinductive, angiogenic, and structural reinforcement properties (Aldhaher *et al*., 2023). No previous study has performed a dedicated bibliometric analysis exclusively focused on alginate-bioactive glass composite systems for bone tissue engineering. Consequently, publication trends, knowledge structure, and emerging research hotspots remain insufficiently characterized. This study addresses this gap by providing a quantitative mapping of the literature and identifying future research opportunities within this rapidly expanding field.

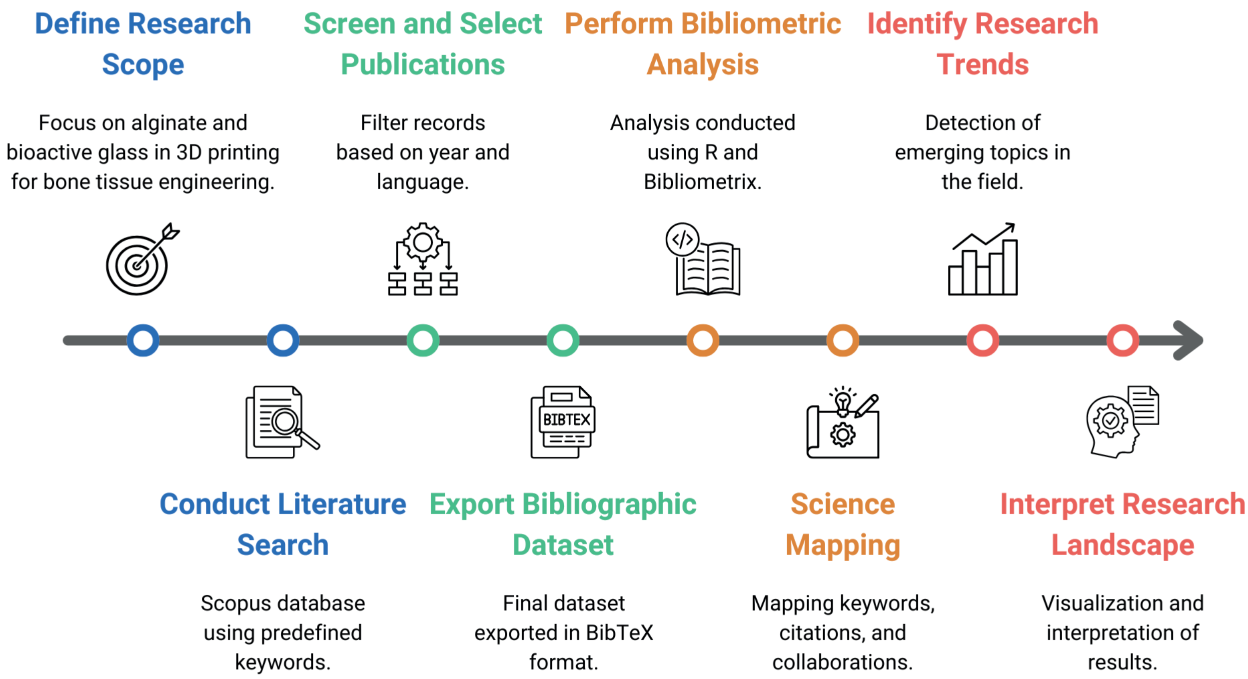
In this context, the present study aims to provide a comprehensive bibliometric analysis of scientific publications indexed exclusively in the Scopus database that address the application of bioactive glass and alginate composite systems in three-dimensional bioprinting for bone tissue engineering. To accomplish this objective, the study first examines the temporal evolution of scientific production and subsequently analyzes the geographical distribution of publications in order to identify global patterns in research activity within this field. Furthermore, the conceptual structure of the literature is investigated through the identification of the most frequent keywords and the construction of expanded keyword co-occurrence networks, which allow the visualization of thematic relationships and the interactions among central research topics. In addition, a citation analysis of the most influential studies is performed to highlight the foundational contributions that have shaped the development of this research area. Finally, the principal findings and emerging trends are synthesized to provide a structured overview of the current scientific landscape and to indicate potential directions for future research.

2 MATERIALS AND METHODS

2. 1 STUDY DESIGN

This study adopted a bibliometric approach to systematically examine the scientific literature concerning the integration of bioactive glass and alginate in additive manufacturing strategies for bone tissue engineering applications. In this context, bibliometric analysis was employed as a structured and quantitative method to (a) investigate the evolution of scientific production, (b) identify emerging research trends, (c) evaluate collaboration patterns, and (d) map the intellectual structure of the field within a defined temporal framework (Xu *et al*., 2023). Furthermore, this approach enables a comprehensive assessment of publication dynamics, thematic development, and knowledge consolidation, thereby providing a robust and reproducible overview of the research landscape (Donthu *et al*., 2021). The overall methodological workflow adopted in this study is summarized in Figure 1.

Figure 1 - Methodological workflow adopted for the bibliometric analysis of sodium alginate and bioactive glass applications in 3D printing for bone regeneration.



Source: Prepared by the author.

2.2 DATA SOURCE AND SEARCH STRATEGY

Bibliographic records were retrieved exclusively from the Scopus database due to its extensive international journal coverage, standardized indexing structure, and comprehensive citation metadata, which collectively contribute to improved data consistency and reproducibility (Guerrero-Bote *et al*., 2021). The search procedure was performed using the advanced search interface available in Scopus and followed a structured Boolean strategy specifically designed to identify studies positioned at the intersection of additive manufacturing, alginate-based biomaterials, and bone tissue engineering involving bioactive glass (Ullah; Asghar; Griffiths, 2023). The final search query was formulated as follows:

(TITLE-ABS-KEY (“printing” OR “printed”) AND TITLE-ABS-KEY (“alginate”) AND TITLE-ABS-KEY (“bone tissue engineering” OR “bone regeneration”) AND ALL (“bioactive glass” OR “bioglass”))

Descriptors related to printing processes, alginate, and bone-related applications were restricted to the Title, Abstract, and Keywords fields in order to ensure thematic specificity and maintain alignment with the central research focus. In contrast, the terms "bioactive glass" OR "bioglass" were searched across all indexed fields, thereby increasing retrieval sensitivity and reducing the likelihood of excluding relevant studies due to variations in indexing practices or reporting formats.

Overall, this structured search strategy was designed to achieve an appropriate balance between precision and comprehensiveness, thus ensuring the identification of studies directly addressing the combined application of bioactive glass and alginate within bone-oriented additive manufacturing approaches.

2.3 INCLUSION AND EXCLUSION CRITERIA

To ensure methodological rigor and alignment with contemporary scientific developments, predefined eligibility criteria were established. Only peer-reviewed documents classified as original research articles, written in English, fully available in their final version, and indexed between 2021 and 2026 were considered for inclusion in the analysis. The temporal delimitation was defined to capture recent advances in biofabrication technologies and composite biomaterial systems, thereby reflecting current research trends in additive manufacturing strategies for bone tissue engineering (He; Yin; Gao, 2023). Furthermore, restricting the document type to original research articles ensured greater consistency in bibliometric indicators and avoided the duplication of synthesized information frequently found in review papers. Accordingly, review articles, conference proceedings, editorials, book chapters, notes, and other non-article formats were excluded from the dataset.

Following data export, duplicate records were identified and removed to avoid the overestimation of publication metrics. Subsequently, titles and abstracts were manually screened to confirm thematic alignment with the established research scope. Only studies explicitly addressing the combined application of alginate and bioactive glass within printing-based fabrication approaches for bone-related applications were retained. Publications that did not clearly demonstrate the integration of both materials in printed constructs intended for bone tissue engineering or regeneration were therefore excluded from the final dataset.

2.4 DATA EXTRACTION AND BIBLIOMETRIC ANALYSIS

All eligible records were exported from the Scopus database in the BibTeX format to preserve complete bibliographic metadata, including authors, countries of affiliation, titles, abstracts, keywords, publication year, source titles, and citation counts (Alviz-Meza *et al*., 2022). Subsequently, the dataset was imported into the RStudio environment (version 4.5.2), where bibliometric analyses were conducted using the Bibliometrix package for both performance evaluation and science mapping (Aria; Cuccurullo, 2017; R Core Team, 2025).

The keyword co-occurrence network was built using the biblioNetwork function of the bibliometrix package (analysis = “co-occurrences”, network = “keywords”). A minimum frequency threshold of 5 occurrences was applied to filter out low-relevance terms and reduce noise in the network. To standardize the co-occurrence matrix and correct for node frequency bias, the Association Strength normalization method was applied. Cluster detection was performed using the Walktrap algorithm, the default community-detection method used by the package. All network visualizations were generated and customized directly within the biblioshiny environment, the graphical interface of the bibliometrix package.

Initially, a descriptive analysis was performed to evaluate the annual scientific production between 2021 and 2026, thereby enabling the identification of temporal trends in the development of the field. In addition, the geographical distribution of research output was examined at the country level based on the institutional affiliations of contributing authors, allowing the identification of national participation patterns within the selected publications. Furthermore, papers’ keywords were analyzed to determine the most frequent and representative terms in the dataset. To investigate the conceptual structure of the research area, a keyword co-occurrence network was constructed using frequency and co-occurrence strength metrics. This analysis enabled the visualization of thematic clusters and the relationships among topics associated with bioactive glass, alginate-based systems, additive manufacturing strategies, and bone tissue engineering applications.

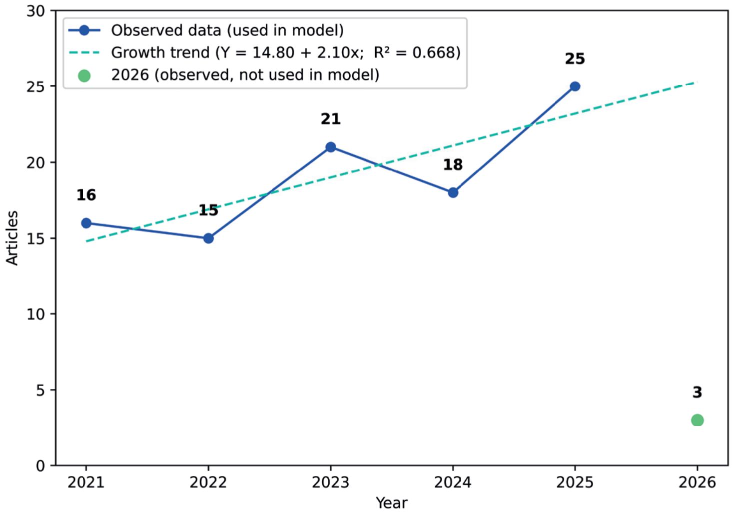
Subsequently, a citation-based performance analysis was carried out as the central component of this study. The ten most cited articles within the dataset were identified and individually examined in order to qualitatively characterize their research focus, material compositions, fabrication strategies, and reported biological or mechanical outcomes. Through this approach, it was possible to obtain a deeper interpretative understanding of the scientific directions and technological advances that have shaped this research domain, thereby complementing the quantitative bibliometric indicators. Finally, for improved data visualization and graphical refinement, the bibliometric outputs were further processed and represented using Python programming language (version 3.12), ensuring greater consistency, clarity, and visual standardization in the generated figures.

3 RESULTS AND DISCUSSION

3. 1 SCIENTIFIC PRODUCTION OVER TIME

A total of 98 articles were identified in the Scopus database during the period from 2021 to 2026, according to the defined inclusion criteria. The temporal distribution of publications demonstrates a progressive growth trend, reflecting the increasing scientific interest in the integration of alginate and bioactive glass within printing-based strategies for bone tissue engineering. As shown in Figure 2, the annual distribution was as follows: 16 publications in 2021, 15 in 2022, 21 in 2023, 18 in 2024, and a peak of 25 articles in 2025. The year 2026 presented 3 publications at the time of data collection.

Figure 2 - Article production over time by Scopus database.



Source: Prepared by the author.

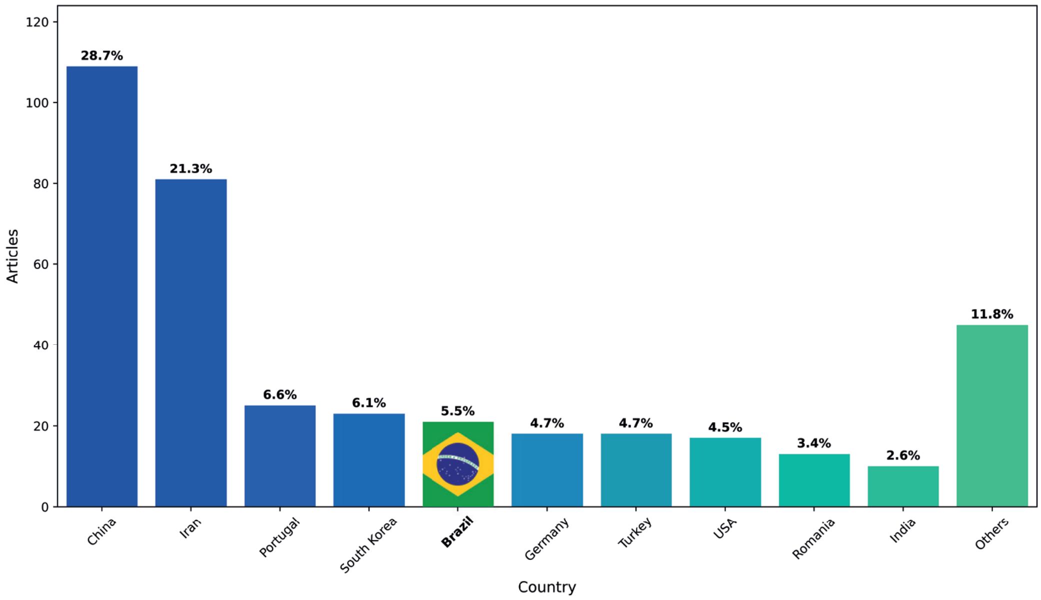
A linear regression model fitted to the data from 2021 to 2025 indicates a consistent upward growth trend in scientific production. The lower number observed for 2026 is attributed to the partial indexing of the year at the time of analysis, rather than a decline in research activity.

Overall, the observed pattern suggests a transition from an initial consolidation phase (2021-2022) to a stage of accelerated expansion beginning in 2023, culminating in the highest output in 2025. This trajectory indicates the strengthening of additive manufacturing approaches incorporating alginate-bioactive glass systems for bone-related applications.

3.2 GEOGRAPHICAL DISTRIBUTION OF SCIENTIFIC PRODUCTION

Figure 3 presents the geographical distribution of scientific publications related to 3D printing of alginate-bioactive glass systems for bone tissue engineering, based on the country of affiliation of contributing authors in the Scopus dataset. The results reveal a global research landscape characterized by a concentration of scientific output in a limited number of countries, alongside broader participation from several emerging contributors.

Figure 3 - Countries by number of publications in the Scopus database (N=380).



Source: Prepared by the author.

China emerges as the leading contributor, accounting for 28.7% of the total publications, followed by Iran (21.3%), which also demonstrates a strong presence in this research field. Together, these two countries represent a substantial portion of the global scientific output, indicating the consolidation of research efforts in regions with significant investment in biomaterials development and additive manufacturing technologies.

A second group of contributing countries includes Portugal (6.6%), South Korea (6.1%), and Brazil (5.5%), each presenting relevant participation within the global research landscape. Notably, Brazil ranks among the leading contributors, highlighting the country's active engagement in the development of advanced biomaterials and biofabrication strategies for bone tissue engineering. This position reflects the growing consolidation of Brazilian research groups in areas such as biomaterials science, regenerative medicine, and additive manufacturing, reinforcing the country's role in the advancement of emerging technologies in biomedical engineering.

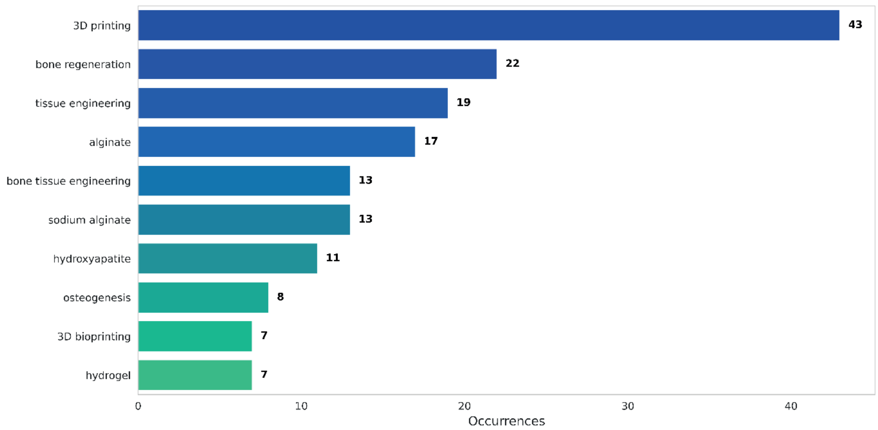
Additional contributions are observed from Germany (4.7%), Turkey (4.7%), and the United States of America (4.5%), indicating participation from technologically advanced research environments with established expertise in additive manufacturing and biomaterial design. Smaller yet noteworthy shares are identified for Romania (3.4%) and India (2.6%), suggesting the progressive expansion of research activity across diverse scientific communities. The category "Others", representing 11.8% of the publications, aggregates contributions from several countries with lower individual publication counts. This distribution indicates that, although the field is led by a limited group of nations, scientific activity is geographically diversified and supported by a broad international network of researchers.

Overall, the geographical distribution indicates that scientific production in this field is primarily driven by countries with strong investments in biomaterials research, additive manufacturing technologies, and biomedical engineering. At the same time, the presence of Brazil among the most representative contributors highlights the relevance of national research in the global context and underscores the increasing participation of Brazilian institutions in the development of innovative strategies for bone tissue regeneration.

3.3 MOST FREQUENT KEYWORDS

Figure 4 presents the most frequently occurring author keywords identified in the analyzed publications. The distribution of these terms provides an overview of the main research themes and highlights the conceptual focus of studies involving alginate-based biomaterials and additive manufacturing for bone tissue engineering.

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



Source: Prepared by the author.

Among all keywords, “3D printing” was the most frequently reported term, with 43 occurrences, emphasizing the central role of additive manufacturing technologies in the development of biomaterial-based scaffolds. The predominance of this keyword reflects the widespread adoption of extrusion-based fabrication techniques to produce customized constructs with controlled architecture and properties suitable for bone regeneration applications.

The second most frequent keyword, “bone regeneration” (22 occurrences), reinforces the primary therapeutic objective of the field, namely the restoration of damaged or defective bone tissue through engineered biomaterials. This is further supported by the high occurrence of “tissue engineering” (19 occurrences) and “bone tissue engineering” (13 occurrences), indicating that the selected studies are largely focused on combining biomaterial design, biological performance, and advanced manufacturing strategies to promote functional bone repair.

Material-related keywords also occupy a prominent position within the dataset. “Alginate” (17 occurrences) and “sodium alginate” (13 occurrences) confirm the relevance of alginate-based polymers as fundamental components of printable bioinks due to their favorable biocompatibility, gelation behavior, and printability. Likewise, the frequent appearance of “hydroxyapatite” (11 occurrences) highlights the importance of incorporating bioactive ceramic phases to improve osteoconductivity and enhance the mechanical and biological performance of composite scaffolds.

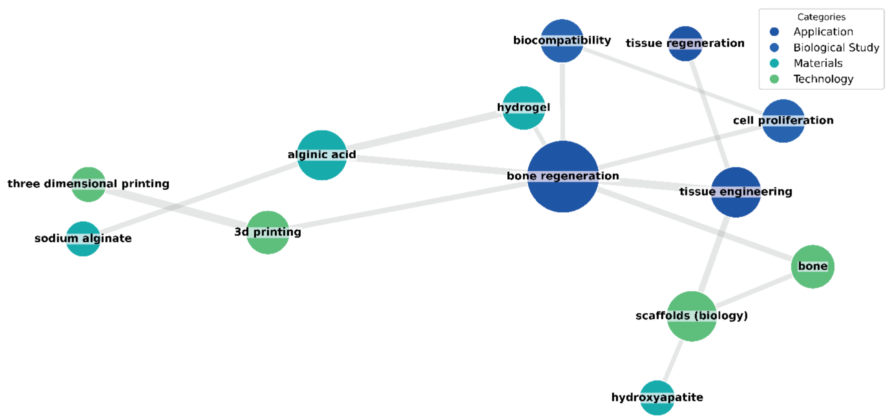
Finally, the occurrence of biological and technological descriptors such as “osteogenesis” (8 occurrences), “3D bioprinting” (7 occurrences), and “hydrogel” (7 occurrences) reflects current efforts to integrate living cells, bioactive matrices, and advanced fabrication techniques into scaffold design. Together, these terms indicate an increasing emphasis on developing multifunctional constructs capable of supporting cell activity, promoting bone formation, and improving regenerative outcomes.

Overall, the keyword distribution reveals a research landscape centered on three complementary pillars: additive manufacturing technologies, alginate-based biomaterials, and bone tissue regeneration. The predominance of these interconnected themes underscores the interdisciplinary nature of the field and highlights the ongoing pursuit of biofabricated scaffolds with enhanced structural, biological, and regenerative performance.

3. 4 EXPANDED CO-OCCURRENCE NETWORKS OF KEYWORDS

Figure 5 presents the expanded keyword co-occurrence network related to research on 3D printing of alginate-bioactive glass systems for bone tissue engineering based on publications indexed in the Scopus database. Unlike simple frequency analyses, co-occurrence networks reveal structural relationships between scientific concepts, illustrating how materials, biological processes, and fabrication technologies interact within the literature.

Figure 5 - Expanded co-occurrence network of keywords related to alginate-bioactive glass systems for bone regeneration.



Source: Prepared by the author.

The first cluster (dark blue - application) is centered on "bone regeneration", "tissue engineering", and "tissue regeneration". In this group, "bone regeneration" stands out as the most central and highly connected node, acting as the main conceptual hub of the network. Its strong links with "tissue engineering" and "tissue regeneration" indicate that the primary focus of the literature is the development of strategies aimed at restoring bone structure and functionality. This cluster clearly reflects the application-driven nature of the research, where biomaterials and fabrication techniques are ultimately directed toward clinical and regenerative outcomes.

The second cluster (medium blue - biological study) includes "biocompatibility" and "cell proliferation". These terms represent key biological evaluation parameters and are directly connected to the application cluster. Their presence highlights that a significant portion of the studies is dedicated to assessing the interaction between biomaterials and biological systems. "Biocompatibility" ensures that materials do not induce adverse responses, while "cell proliferation" indicates their ability to support cell growth and tissue formation. This cluster reinforces the importance of validating the biological performance of developed constructs.

The third cluster (light blue - materials) comprises "hydrogel", "alginic acid", "hydroxyapatite", and "sodium alginate". This group reflects the material composition and formulation aspect of the research field. The close association between "alginic acid" and "sodium alginate" emphasizes the central role of alginate-based polymers as hydrogel matrices. The presence of "hydrogel" indicates their use as carriers for cells and bioactive agents, while "hydroxyapatite" points to the incorporation of inorganic phases to enhance osteoconductivity and mechanical properties. The proximity of this cluster to the central node suggests that material selection is crucial for enabling successful bone regeneration applications.

The fourth cluster (green - technology) includes "bone", "scaffolds (biology)", "3D printing", and "three dimensional printing". This cluster represents the technological and fabrication dimension of the network. The strong connections between "3D printing" and "scaffolds (biology)" highlight additive manufacturing as a key tool for producing biomimetic structures. The association with "bone" indicates that these technologies are specifically tailored for bone-related applications. This cluster demonstrates how advanced fabrication techniques enable precise control over scaffold architecture, which is essential for guiding tissue regeneration.

Overall, the co-occurrence network reveals a strongly interdisciplinary structure integrating materials science, additive manufacturing, and regenerative medicine. The central role of "bone regeneration", combined with its connectivity to alginate-based hydrogels, scaffold fabrication, and biological evaluation parameters, indicates that research in this field is oriented toward the development of multifunctional biomaterial systems capable of supporting bone repair. These relationships illustrate how advances in hydrogel-based bioinks and "3D printing" technologies are converging to enable the rational design of scaffolds tailored for bone tissue engineering applications.

3.5 BIBLIOMETRIC ANALYSIS AND LEADING CONTRIBUTIONS

To complement the bibliometric indicators obtained from the database search, Table 1 summarizes the ten most influential and highly cited studies addressing the integration of sodium alginate with bioactive glass or silicate-based bioceramics in 3D printing strategies for bone tissue engineering (BTE). These studies represent the most relevant scientific contributions within the analyzed dataset and collectively illustrate the technological evolution of alginate-based composite scaffolds used in 3D printing strategies for bone tissue engineering.

Table 1 - Most cited articles on alginate-based composite scaffolds used in 3D printing strategies for bone tissue engineering identified in the Scopus database.

AUTHOR/ YEAR	TITLE	JOURNAL	DOI	N° CITATIONS
Guo, L. (2021)	The role of natural polymers in bone tissue engineering	Journal of Controlled Release	10.1016/j.jconrel.2021.08.055	314
Dutta, S. (2021)	3D-printed bioactive and biodegradable hydrogel scaffolds of alginate/gelatin/cellulose nanocrystals for tissue engineering	International Journal of Biological Macromolecules	10.1016/j.ijbiomac.2020.12.011	205
Nie, R. (2022)	3D printing of MXene composite hydrogel scaffolds for photothermal antibacterial activity and bone regeneration in infected bone defect models	Nanoscale	10.1039/d2nr02176e	151
Monavari, M. (2021)	3D printing of alginate dialdehyde-gelatin (ADA-GEL) hydrogels incorporating phytotherapeutic icariin loaded mesoporous SiO_2-CaO nanoparticles for bone tissue engineering	Materials Science & Engineering C	10.1016/j.msec.2021.112470	109
Mi, X. (2022)	3D printing of Ti3C2-MXene-incorporated composite scaffolds for accelerated bone regeneration	Biomedical Materials	10.1088/1748-605X/ac5ffe	84
Yang, C. (2021)	3D Printed Enzyme-Functionalized Scaffold Facilitates Diabetic Bone Regeneration	Advanced Functional Materials	10.1002/adfm.202101372	84
Chai, N. (2021)	Construction of 3D printed constructs based on microfluidic microgel for bone regeneration	Composites Part B	10.1016/j.compositesb.2021.109100	77
He, Y. (2022)	Remote control of the recruitment and capture of endogenous stem cells by ultrasound for *in situ* repair of bone defects	Bioactive Materials	10.1016/j.bioactmat.2022.08.012	71
Hu, X. (2024)	Progress in the application of 3D-printed sodium alginate-based hydrogel scaffolds in bone tissue repair	Biomaterials Advances	10.1016/j.bioadv.2023.213501	62
Liu, C. (2021)	3D Printed Gelatin/Sodium Alginate Hydrogel Scaffolds Doped with Nano-Attapulgite for Bone Tissue Repair	International Journal of Nanomedicine	10.2147/IJN.S339500	61

Source: Prepared by the author.

The selected studies reveal that alginate-based systems are rarely used as isolated materials. Instead, they are commonly combined with bioactive inorganic phases, including bioactive glass, silicate nanoparticles, hydroxyapatite, and tricalcium phosphate, in order to overcome the intrinsic limitations of alginate hydrogels, such as limited mechanical strength and poor cell adhesion.

It is worth noting that the bibliometric analysis (e.g., top-cited studies) identified few foundational articles with a broader scope, such as studies on natural polymers and multifunctional platforms. Although these works do not focus exclusively on the 3D-printed bioactive glass-alginate combination, they were retained in the qualitative analysis because they constitute the theoretical and conceptual framework mapped within the scientific ecosystem of this field.

Among the most cited studies, Guo *et al*. (2021) provide a comprehensive overview of the role of natural polymers in bone tissue engineering, highlighting alginate as a versatile hydrogel matrix capable of supporting cell encapsulation and printable bioinks. However, the authors emphasize that the biological performance of alginate scaffolds is significantly enhanced when combined with bioactive ceramics capable of stimulating osteogenesis and vascularization. Several experimental investigations focus on improving the mechanical stability and bioactivity of alginate-based scaffolds. For instance, Dutta *et al*. (2021) developed 3D-printed hydrogel scaffolds composed of alginate, gelatin, and cellulose nanocrystals (CNCs). The incorporation of CNCs acted as a reinforcing phase, improving compressive strength and promoting enhanced mineralization behavior, which is essential for bone tissue regeneration.

Similarly, Liu *et al*. (2022) investigated alginate/gelatin hydrogels doped with nano-attapulgite, a magnesium silicate nanomaterial. Their results demonstrated improved printability, structural stability, and osteogenic potential, including enhanced mineral deposition and successful bone regeneration in a rabbit tibial defect model. More advanced hybrid systems have also been explored. Monavari *et al*. (2021) developed alginate dialdehyde-gelatin (ADA-GEL) hydrogels incorporating mesoporous SiO_2-CaO nanoparticles. These nanoparticles are described as bioactive glass components capable of releasing biologically active ions while simultaneously serving as drug delivery platforms for osteogenic molecules such as icariin. The study reported improved scaffold bioactivity and enhanced differentiation of osteoblast-like cells.

Another relevant line of research involves the incorporation of two-dimensional nanomaterials. Nie *et al*. (2022) and Mi *et al*. (2022) explored the use of Ti_3C_2 MXene nanosheets in alginate-based composite scaffolds. These materials are reported to introduce photothermal antibacterial properties and enhance osteogenic differentiation, enabling multifunctional scaffolds capable of simultaneously preventing infection and promoting bone regeneration. In addition to structural and biological optimization, some studies address disease-specific therapeutic strategies. For example, Yang *et al*. (2021) developed an enzyme-functionalized scaffold capable of regulating the local microenvironment in diabetic bone defects. According to the reported findings, immobilization of glucose oxidase and catalase within alginate-based matrices reduces oxidative stress and promotes vascularization, ultimately improving bone regeneration under diabetic conditions.

Another emerging approach focuses on cell protection during the printing process. Chai *et al*. (2021) proposed microfluidic microgel-based bioinks consisting of a collagen core encapsulated by an alginate shell. This configuration was reported to significantly improve cell survival during extrusion-based bioprinting by protecting cells from shear stress. Finally, He *et al*. (2023) introduced an innovative scaffold system capable of remotely controlling stem cell recruitment through ultrasound stimulation. In this design, alginate-based matrices are used as carriers for growth factors such as stromal cell-derived factor-1 (SDF-1) and bone morphogenetic protein-2 (BMP-2), enabling on-demand release and supporting *in situ* bone regeneration. Collectively, these studies demonstrate that the development of alginate-based scaffolds for bone tissue engineering is increasingly centered on multicomponent systems integrating polymeric matrices, bioactive ceramics, and functional nanomaterials, highlighting the transition toward multifunctional regenerative platforms.

3.6 PRINCIPAL FINDINGS AND TRENDS

The synthesis of the most influential studies summarized in Table 1 reveals several converging trends that characterize the evolution of 3D-printed alginate-based scaffolds for bone tissue engineering. First, a clear research direction involves the development of hybrid organic-inorganic scaffolds designed to mimic the hierarchical structure of natural bone tissue. Since bone consists of both an organic matrix and a mineral phase, the integration of alginate with bioactive ceramics such as bioactive glass, hydroxyapatite, and β-tricalcium phosphate has become a widely adopted strategy. These composites have been widely investigated because they are reported to improve mechanical strength, stimulate osteogenic differentiation, and enhance hydroxyapatite formation.

Furthermore, advances in bioink engineering and printability optimization have significantly improved the structural fidelity and biological performance of printed scaffolds. The analyzed studies frequently report that reinforcement strategies involving nanomaterials such as cellulose nanocrystals, nano-attapulgite, and mesoporous silica nanoparticles enhance viscosity, mechanical stability, and mineralization capacity while maintaining favorable rheological properties for extrusion-based printing. Besides that, the field is increasingly moving toward the design of multifunctional and smart scaffolds capable of addressing multiple biological challenges simultaneously. Examples reported in the analyzed literature include scaffolds incorporating photothermal MXene nanomaterials for antibacterial activity, enzyme-functionalized matrices designed for diabetic bone regeneration, and stimulus-responsive systems capable of releasing growth factors under external triggers such as ultrasound.

Another important trend concerns the integration of biological signaling strategies into scaffold design. Instead of relying solely on transplanted cells, several studies now focus on recruiting endogenous stem cells through chemotactic factors or controlled release systems, promoting *in situ* regeneration and potentially improving clinical translation. Finally, vascularization has emerged as a critical factor for successful bone regeneration. The analyzed literature consistently highlights the incorporation of bioactive ions released from silicate-based materials, particularly calcium and silicon species, as a strategy to stimulate angiogenesis and improve tissue integration.

Overall, these findings indicate that research in alginate-based 3D printed scaffolds is evolving from simple structural matrices toward complex bioactive platforms capable of simultaneously providing mechanical support, biological signaling, and therapeutic functionality. Future developments are expected to focus on improving scaffold vascularization, achieving precise control of degradation kinetics, and advancing clinically translatable biofabrication strategies.

It is important to acknowledge that the present bibliometric analysis was based exclusively on the Scopus database. Although Scopus provides broad international coverage and standardized citation metadata, relevant publications indexed exclusively in other databases, such as Web of Science or PubMed, may not have been captured. Therefore, the findings presented here should be interpreted as representing the scientific landscape indexed in Scopus rather than the entirety of the global scientific literature.

CONCLUSIONS

This bibliometric study demonstrates that research on bioactive glass-alginate composites for 3D printing in bone tissue engineering has entered a phase of rapid scientific consolidation, driven by the growing demand for biomaterials capable of combining printability, mechanical reinforcement, and biological functionality. Rather than representing isolated advances in scaffold fabrication, the analyzed publications indicate a progressive shift toward integrated strategies that combine materials engineering, additive manufacturing, and regenerative medicine.

The findings show that alginate is consistently employed as part of multifunctional composite systems rather than as a standalone biomaterial, highlighting the importance of incorporating bioactive inorganic phases to overcome its intrinsic limitations and enhance osteogenic performance. At the same time, the literature reveals that current research priorities extend beyond scaffold fabrication to include antibacterial activity, controlled therapeutic delivery, angiogenesis, and in situ tissue regeneration, reflecting the increasing complexity of biofabricated constructs.

Overall, this study provides a quantitative overview of the current scientific landscape and identifies the main directions guiding the evolution of the field. These findings suggest that future advances in bone tissue engineering will rely on the development of multifunctional composite bioinks with improved biological performance and greater translational potential, contributing to the advancement of clinically applicable strategies for bone repair and regeneration.

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