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A scientometric assessment of titanium-hydroxyapatite composite

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Abstract

In orthopaedic and dental implants, a bone graft has been widely used as a metal material because of its excellent mechanical properties. One of the materials used as an implant is titanium because of low modulus elasticity and corrosion resistance. However, using metal as an implant material has its drawbacks because it has low bonding strength within bone tissue. Combining titanium and hydroxyapatite into a composite has been becoming an option to increase implant materials' bioactivity. Bibliometric analysis was conducted to find trends and contributions to titanium-hydroxyapatite composite research. About 932 documents on articles and reviews of Ti–HA composite were obtained from the SCOPUS. Exported data in CSV format were processed using VOS-viewer and Biblio-shiny to visualize annual scientific contributions, corresponding authors' country, top published and top citation country and sources, top-citation affiliations and documents, also co-occurrence of all keywords by authors. China became the most publications document, and Sichuan University became the most relevant affiliation. From all sources, Biomaterials have the highest h-index of 32, with citations of 10,834 papers. The main topics from the authors' keywords are "hydroxyapatite" and "composite coatings." Research related to titanium hydroxyapatite composite has prospects for further development to be used in biomedical applications.

Keywords: bibliometric analysis, composite, titanium, hydroxyapatite, SCOPUS

1. Introduction

In biomedical applications, implant materials for orthopaedics and dental became a concern for researchers. Bone graft was a general method for orthopaedic surgery procedures [1]. To fulfil the requirements, implant materials should be biocompatible and not harmful to the human body [2]. Besides, an implant must be osteoconductive material that can increase the osteogenic, leading to bone regeneration [3]. Implant material was also not cytotoxic, which could be caused by increasing ions in the blood [2]. In addition to biological properties, implant materials that have a function as a permanent bone graft must have high modulus elasticity to support all the loads [4].

Metals are a material that is widely used in implants because of their excellent mechanical properties, like stainless steel, Co-Cr alloys, titanium, and its alloy [5]. However, titanium and its alloy had a lower modulus elasticity than other metals, 110 – 117 GPa [6], low density, and high corrosion resistance in physical conditions [7]. The difference in modulus elasticity with human bone (4 – 30 GPa) [6] caused stress-shielding in the implant area [8]. Besides stress-shielding, the metal interface of the implant materials has low bonding strength resulting in bone resorption, poor osseointegration, and limited long-term fixation [8]. Therefore, additional materials were needed to increase the bioactive properties of implant materials [9].

Hydroxyapatite has similar properties to human bone structures [10]. Hydroxy-apatite, with a Ca/P ratio of 1.67, is a calcium apatite with the chemical structure $Ca_{10}(PO_4)_6(OH)_2$ [11]. Hydroxyapatite has excellent biocompatibility, in the organic parts of bones and teeth of humans. Therefore, it can be attached to bone tissues [12]. Titanium combined with hydroxyapatite into a composite was expected to increase the bioactivity of implant materials [13]. Various studies of titanium hydroxyapatite composites have been conducted for more than twenty years. There also have been many article reviews on implant materials, including reviews of titanium and hydroxyapatite, separately. The articles covered several methodologies to produce Ti-HA composite, the physical and chemical effect of combining materials, mechanical strength, and biological evaluations of implant materials. Amir Arifin summarizes the methods of making Ti-HA compo-sites using the powder metallurgy process and the interaction between titanium and hydroxyapatite after in vitro and in vivo tests [2].

A.R. Rafieerad reviewed plasma electrolytic oxidation as a method to coat biomedical grade titanium using calcium phosphate composite to outline the corrosion behaviour, microstructure, morphology, and crystallinity [14]. P.A. Ramires studied titanium-hydroxyapatite coating composite with the sol-gel method to observe its bio-compatibility through cytotoxicity testing using human MG63 osteoblast-like cells [15]. However, bibliometric analysis on titanium hydroxyapatite composite has never been published in the last twenty years. Bibliometric is a statistical analysis method on published documents [16]. This method was used to assess various aspects of the topic [17]. Bibliometric analysis is used a lot across multiple research areas, such as nanotechnology [18], 3D printing [19], food chemistry [20]; and information technology [21].

The purpose of the bibliometric analysis of titanium hydroxyapatite composite is to find out the research trends of a particular topic, the top citation documents, and their impact globally. Also, it is helpful for other researchers and annual contributions from affiliates and authors of a research field [22]. In this work, the database used is SCOPUS. The period of the documents search was limited from 2000 – to June 4th, 2022. VOS-viewer and Biblio-shiny analysed the 932 documents as a tool for bibliometric analysis of titanium hydroxyapatite composite.

2. Methods

Data Source

This review was based on a publication related to titanium-hydroxyapatite composite for the last twenty years, from 2000 until June 6th, 2022. The data were extracted from the SCOPUS database (by Elsevier). The reason for choosing SCOPUS to perform the bibliometric analysis is because it stores many documents for the Engineering category. Hence, the number of papers was higher than in other databases [23]. Furthermore, SCOPUS provided international collaboration by counting the authors' articles from the same country and different countries [17]. Therefore, this review analyses authors, journals, countries, keywords, and references.

The methodology for searching the documents was carried out through several stages: entering the keywords, then searching and collecting data from the SCOPUS database in CSV format [23]. The formula for document searched was (titanium AND hydroxyapatite AND composite) in search within article title, abstract, keywords as documents category. The document limitations were the publication stage, publication year, subject area, language, and document type. All manuscripts published in English, using subject area limitation only on Material Science and Engineering with a journal and review as a document type.

Methodology

Documents results obtained from the SCOPUS database using the formula above were selected for all. All items such as citation information (authors, document title, year, EID, source title, volume, issues, pages, citation count, source & document type, publication stage, DOI, open access); bibliographic information (affiliations, ISSN, publisher, editors, language, correspondence address, abbreviated source title); abstract & keywords (abstract, author keywords, index keywords); funding details (number, acronym, sponsor, funding text); and other information (tradenames, accession numbers, journal information, references) were converted into CSV format.

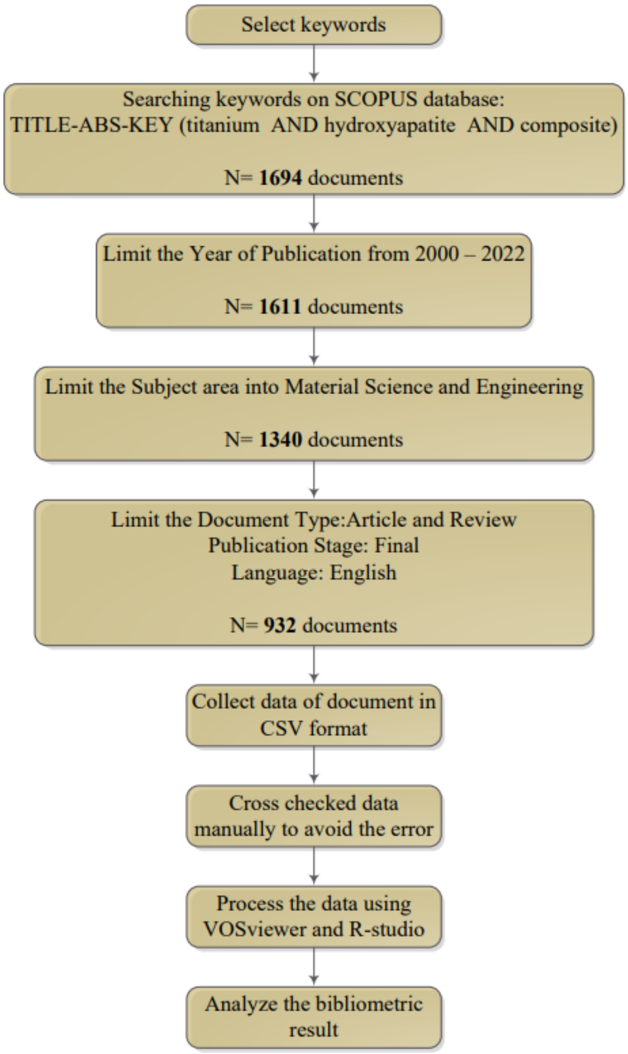


Figure 1. Flow chart process of bibliometric review

VOS-viewer software version 1.6.18 (Leiden University, Netherlands) was used to generate co-authorship, co-occurrence, citations, and co-citations to visualize similarities. VOS-viewer is used because of its simplicity, flexibility, and precise results [24]. Other software, such as Microsoft Excel and Biblio-shiny (K-Synth Srl, Naples, Italy), was used to show several categories by the SCOPUS database. A flow chart of the methodology of searching and processing the data can be seen in Figure 1.

3. Result and Discussion

Annual Publications and Contributions

The total number of published documents from the SCOPUS database is 932 documents. Research on titanium hydroxyapatite composite was initiated by Asano, Kazuko, Ichiko, Tadatoshi, Tonegawa, and Hiroshi in 1982 with the title "Development of Hydroxyapatite–Titanium Composite Material as an Implant Material." From a total of 932 documents collected from articles and reviews as a document type, articles were the most frequently published documents with 94.96% or 885 records, followed by review papers with 5.04% or 47 records. From 2000 – 2022, 247 sources originate from journals, books, book series, proceedings, etc.

Several publications on titanium hydroxyapatite composite per year from 2000 until 2022 are shown in Figure 2. In the last twenty years, publications on titanium hydroxyapatite composite have experienced an increase with fluctuating conditions between 2008 and 2019. The peak year of document publication in titanium hydroxyapatite composite was 2021, with a total output of 84 documents. With an increasing trend from 2000 to 2022, it shows that demand for material implants from mixing materials such as titanium as metal and hydroxyapatite as a bio-ceramic is an essential topic in biomedical applications to improve the mechanical and biological properties. When the data was collected, the achievement of 2022 has not yet finished.

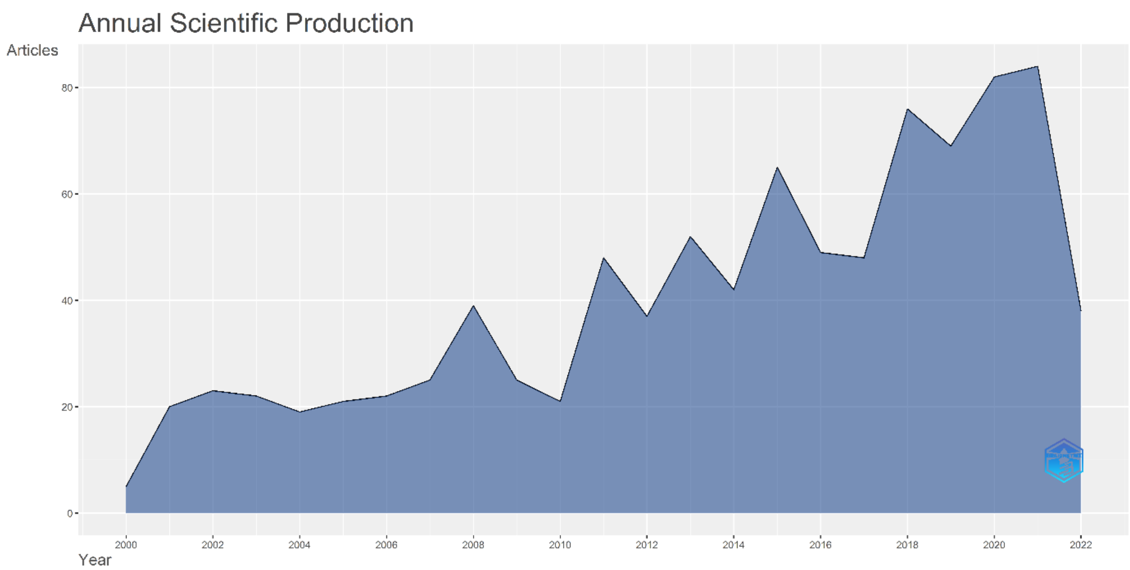


Figure 2. Publication of titanium hydroxyapatite composite by year (2000 – June 6th, 2022)

Many authors from different countries worldwide have studied to explore combining two materials with various materials and contributing to the publication of articles and reviews. As a result, a total of 932 documents from 57 countries contributed to the publication of titanium hydroxyapatite composite, and the top 15 countries are shown in Figure 3.

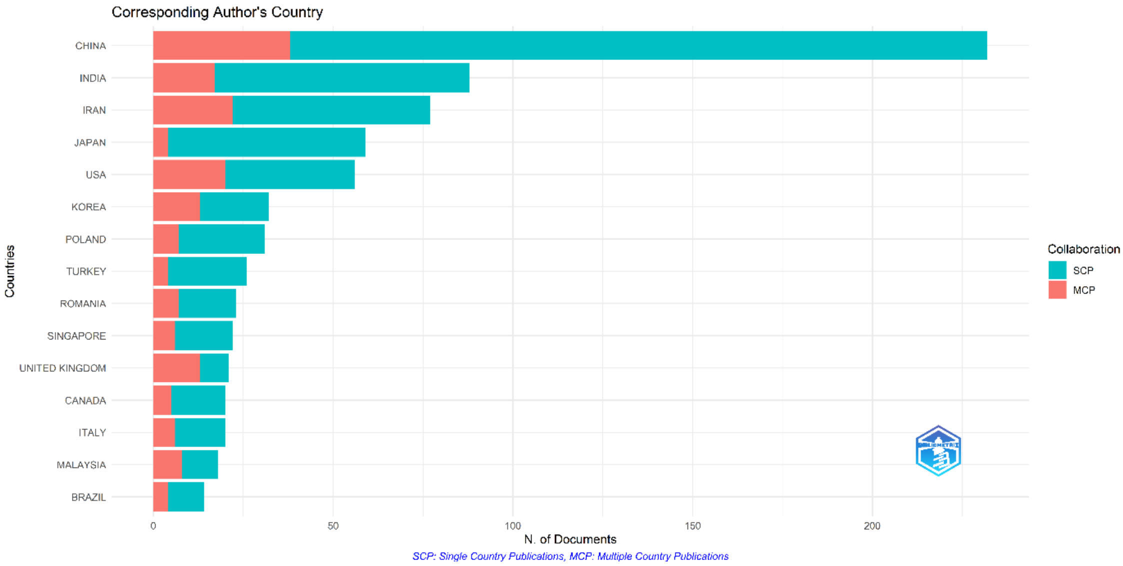


Figure 3. Top 15 countries with published articles

China contributed the most publications with 232 documents or 24.89%, and India published 88 papers or 9.44%, consisting of both single-country publications (SCP) and multiple-country publications (MCP). The single-country publication was an article whose authors came from the same country and represented intra-country collaboration. In contrast, numerous country publications published articles whose authors came from several countries and represented inter-country collaboration [17]. This result was followed by Iran, Japan, and the USA, which have published over 50 documents over the last twenty years.

Total publications and citations of the top 15 countries can be seen in Table 1. Even though China has many published articles, the total citations over the years were lower than the USA, with 8,536 cited documents, followed by China, with 6,335 papers. This data indicates that the United States had a significant influence on titanium hydroxyapatite composite research. However, some regions, such as Africa, Southeast Asia, and the Middle East, have few articles. The total citations are up to 32,957 documents over the years, with an average citation of documents was 51.61, and the average citation of the year was 4.68.

Table 1. Total publications and total citations from top 15 countries

Country	TP	TC
China	232	6,335
India	88	1,779
Iran	77	1,884
Japan	59	3,332
USA	56	8,536
Korea	32	1,370
Poland	31	332

Country	TP	TC
Turkey	26	650
Romania	23	275
Singapore	22	1,140
United Kingdom	21	1,346
Canada	20	519
Italy	20	1,332
Malaysia	18	530
Brazil	14	288

*TP= total publications; TC: total citations

The most relevant affiliations of published documents between 2000 – 2022 can be seen in Figure 4. From 57 countries, a total of 999 alliances from authors contributed to this posted subject. During the last twenty years, Sichuan University, Chengdu, China, was the most relevant affiliation with 99 authors. This result was followed by Nanyang Technological University, Singapore, and the University of Belgrade, Serbia, with 51 and 48 authors, respectively. Asia has most affiliates that appear in the top 15 affiliations categories, such as Sichuan University, Nanyang Technological University, Sahand University of Technology, Hebei North University, Huazhong University of Science and Technology, Iran University of Science and Technology, Universiti Kebangsaan Malaysia, Islamic Azad University, University of Electronic Science and Technology of China, South China University of Technology, Jilin University, and Tohoku University. Europe has several affiliates to contribute, i.e. University of Belgrade and Agh University of Science and Technology, and affiliation from America, Northeastern University.

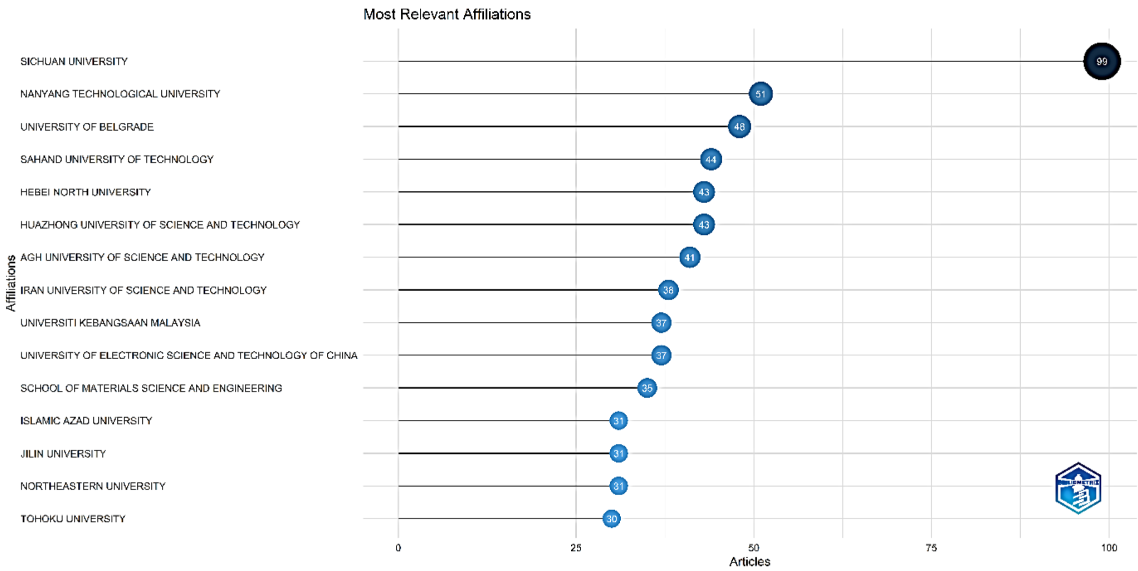


Figure 4. Most relevant top 15 affiliations of titanium hydroxyapatite composite

Since the first documents about titanium hydroxyapatite composite began in 1982, there are 247 published sources. The most published sources are Surface and Coating Technology, with 63 papers. Most citations from the top 15 sources are Biomaterials, with Elsevier as a publisher. It is followed by Materials Science and Engineering C, Surface and Coating Technology, Ceramics International, and Applied Surface Science with 2,071; 1,838; 1,456; and 1,436 total citations, respectively.

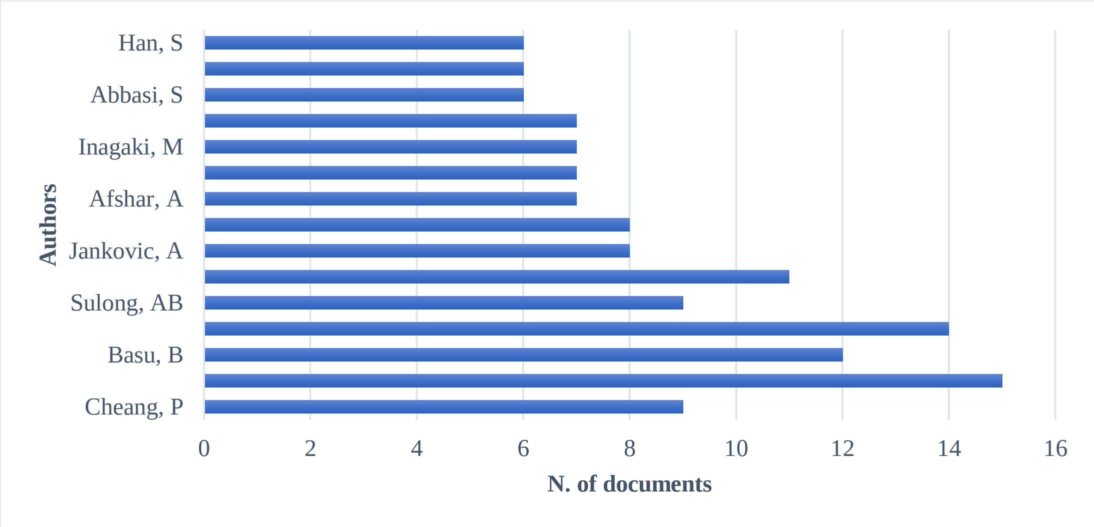
Total publications, citations, and h-index from the top 15 sources can be seen in Table 2. The h-index is used as an analysis because it has an indicator that combines the impact and productivity of articles [18]. The source with the highest h-index was Biomaterials, with 32. It is related to a total of citation documents because indicators in bibliometric analysis evaluated the impact of research more effectively [20]. In this case, Surface and Coatings Technology ranked 3rd on the h-index (27) and total citation (1,838) documents, even though the total publications were in the 1st rank. In another case, for example, the Journal of Biomedical Materials Research – Part B Applied Biomaterials had an h-index of 14 with a total citation of 600 documents, even with a total publication of 19 papers. It means that these sources had productivity and a great impact on other research by other authors.

Table 2. Total publications and citations from the top 15 sources

Sources	TP	TC	H Index	IF
Surface and Coatings Technology	63	1,838	27	4.158
Materials Science and Engineering C	59	2,071	30	7.328
Ceramics International	57	1,456	24	4.473
Applied Surface Science	39	1,436	26	6.707
Biomaterials	34	10,834	32	12.48
Journal of Materials Science: Materials in Medicine	33	1,137	21	3.896
Journal of Biomedical Materials Research - Part A	30	1,170	19	4.396
Journal of The Mechanical Behavior of Biomedical Materials	21	367	11	3.902
Materials	21	217	8	3.623
Materials Letters	21	556	12	3.423
Journal of Biomedical Materials Research - Part B Applied Biomaterials	19	600	14	3.368
Acta Biomaterialia	14	757	13	7.242
Materials Chemistry and Physics	14	222	7	4.56
ACS Applied Materials and Interfaces	12	423	8	9.229
Transactions of Nonferrous Metals Society of China (English Edition)	11	96	6	2.917

*TP= total publications; TC= total citations; IF= impact factor.

Authors Contributions



Graph 1. Most contributed authors

There is a total of 3,266 authors contributed to the publications. Graph 1 shows the top 15 most contributed authors. Dr. Khiam Aik Khor (Singapore), Dr. Jafar Khalil-Alafi (Iran), and Dr. Bikramjit Basu (India) are the most productive authors with 15, 14, and 12 documents, respectively. The study about titanium hydroxyapatite composite by Dr. Khiam Aik Khor with the title "In vitro studies of plasma-sprayed hydroxyapatite/Ti-6Al-4V composite coatings in simulated body fluid (SBF)" in 2003 got about 215 total citations [25].

The top 15 most globally cited documents are shown in Figure 5. Citation is one of the analytical methods in bibliometrics to determine the impact and recognition of a document. Articles that get a high number of citations can help to find the author's contribution to revealing research results [18]. Among all the documents, review articles by Vassilis Karageorgiou with the title "Porosity of 3D biomaterial scaffolds and osteogenesis" got 4563 total citations. This review article discusses the effect of porosity and pore size of scaffolds. By biological evaluations, scaffolds with high porosity volume resulted in good bone ingrowth. However, the porosity of scaffolds will have a high void volume, so the mechanical properties will decrease. Therefore, it is necessary to use a new fabrication method to obtain the recommended pore size > 300 µm [26].

Another top citation document by Tadashi Kokubo with the title "Novel bioactive materials with different mechanical properties" in 2003 discussed using bioactive ceramics materials to integrate with living bone in biomedical applications, getting 1600 total citations. This article shows that ceramic bioactive materials with functional groups such as Si-OH, Ti–OH, Zr–OH, Nb–OH, Ta–OH, –COOH, and PO_4H_2 can induce the formation of new apatite similar to human bone [27]. The top 3 citation documents by Thomas J. Webster in 2004 with the title "Increased osteoblast adhesion on nanophase metals: Ti, Ti6Al4V, and CoCrMo". Based on the result of this research, it is known that implant materials made from metal nanophases can increase biological activity by adhering osteoblasts to the particle boundaries. Continuous adhesion processes, such as the deposition of calcium-containing minerals, show promising results in orthopaedic applications [28].

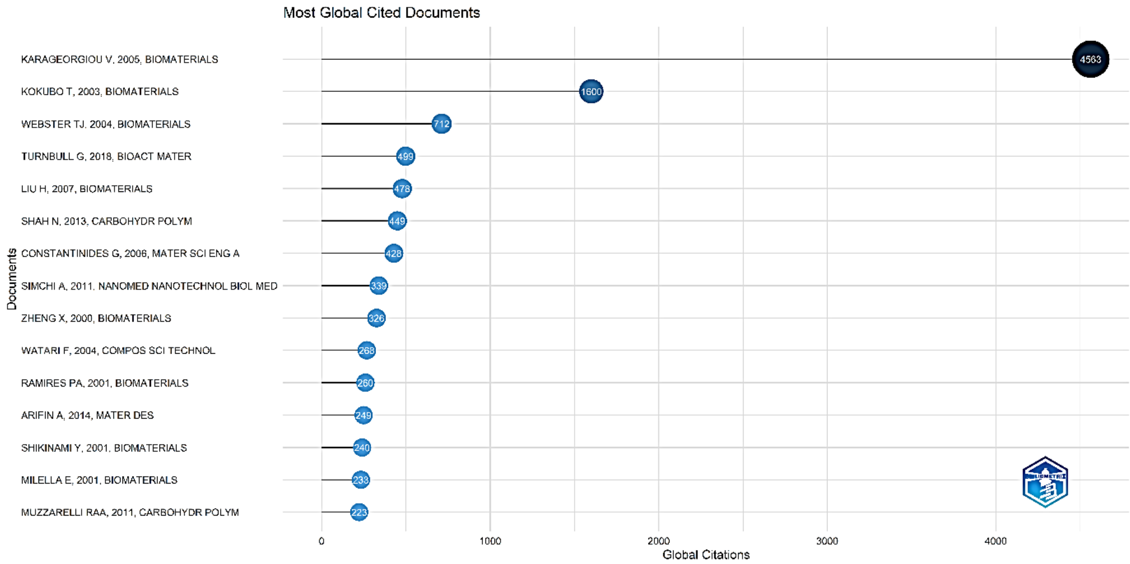


Figure 5. Top 15 most global cited documents

Co-occurrences by Authors

In keyword analysis, the frequency of occurrence is an indicator of the strength of keywords which can be to find out the topics in the research [29]. Figure 6 shows occurrences from all keywords for titanium hydroxyapatite composite research using VOSviewer with 10 minimum occurrences of a keyword. Of the 7780 total keywords, 479 occurrences meet the threshold. In Figure 6, every circle represented one keyword, and every circle size represented the impact of the keyword. Every cluster is divided into specific colors, where is cluster 1 the highest cluster represented by red color. Cluster one is the most keywords related to titanium hydroxyapatite composite research.

A line is connected between keywords in every cluster and between keywords in different clusters. The lines represented the networking of keywords with other keywords, which showed the relations of the keywords. For example, the largest circle belongs to the "hydroxyapatite" keyword, the most networking keyword on another with 6508 total link strength. Apart from hydroxyapatite, a keyword that is quite widely used in research is "composite coatings", where many studies were conducted to research the used metal implant materials coated with hydroxyapatite, as well as other composite materials with bioactive properties. One of the most cited articles on composite coatings research is by Xuebin Zhang, Minhui Huang, and Chuanxian Ding with the title Bond strength of plasma-sprayed hydroxyapatite/Ti composite coatings in 2000, which discussed titanium hydroxyapatite composite as a coating on Ti6Al4V alloy substrate with atmospheric plasma spraying method [30].

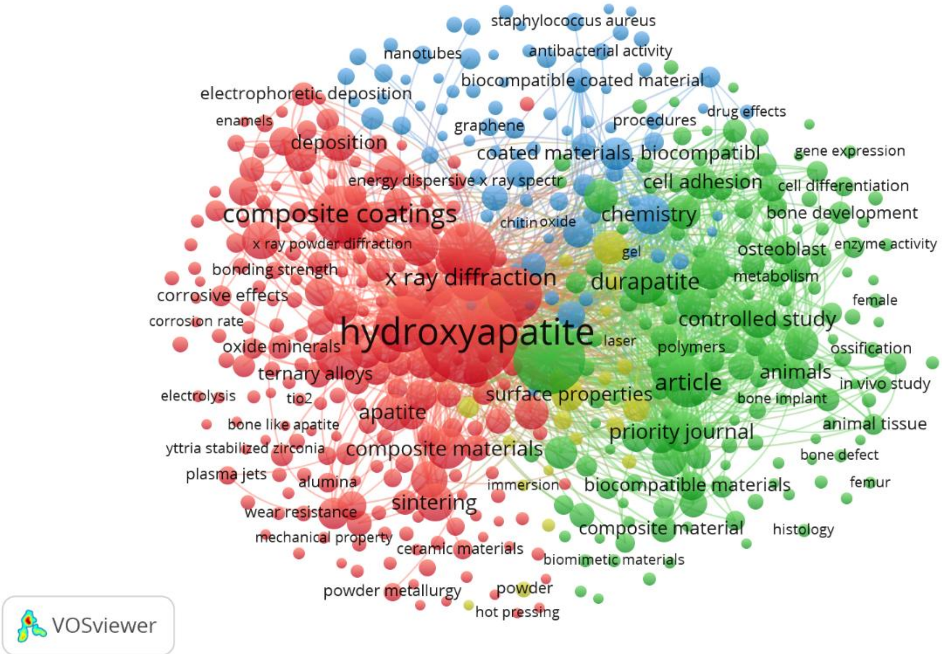


Figure 6. Co-occurrence of all keywords in the research of titanium hydroxyapatite composite

In several studies, hydroxyapatite combines with other materials such as polymers, ceramics, chitosan, etc. Because it combines two or more materials with different properties, many studies carried out the chemical characterization of composite to determine the safety of implant material in the human body. One of the widest characterization methods is "x-ray diffraction" (XRD) testing, which also showed a large circle size and appeared at cluster 1 in Figure 6. Article titled "Preparation and characterization of titania/hydroxyapatite composite coatings obtained by sol-gel process" by E. Milella, F. Cosentino, A. Licciulli, and C. Massaro in 2001 used x-ray diffraction (XRD) as a measurement of hydroxyapatite powder and hydroxyapatite–titania composite coating [31].

Several materials are used as a composite from 932 documents from the SCOPUS database. The most used materials are shown in Figure 7. Besides hydroxyapatite and titanium as the primary initial materials, some materials can be used as an additive to form a composite. The material selection is carried out by considering the safe constituent material for the human body and good bioactivity properties to stimulate the growth of the new apatite layer and bone regeneration. Additive materials can be metals, polymers, proteins, and bio-ceramics.

A review article by Riccardo A.A. Muzzarelli with the title "Chitosan composites with inorganics, morphogenetic protein, and stem cells, for bone regeneration in 2011 got 223 total citations. This article reviews bio-polymer material to regenerate bone lost because of disease or trauma. Chitosan had good biocompatibility and an excellent response to promote cell adhesion and proliferation. Many studies research the technological and chemicals of chitosan to produce the composite [32].

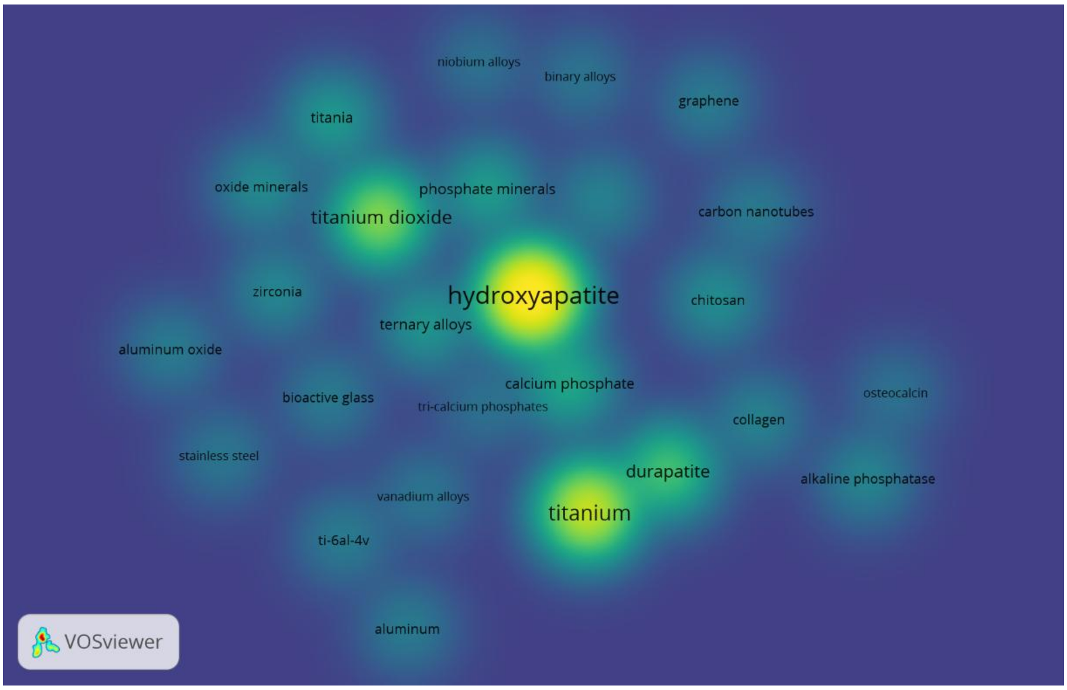


Figure 7. Various materials used in titanium hydroxyapatite composite studies

In 2014, Li, Ming; Liu, Qian; Jia, Zhaojun; Xu, Xuchen; Cheng, Yan; Zheng, Yufeng; Xi, Tingfei; and Wei, Shicheng published an article entitled "Graphene oxide/hydroxyapatite composite coatings fabricated by electrophoretic nanotechnology for biological applications." This document discussed a composite made of graphene oxide (GO) and hydroxyapatite coatings on a titanium substrate by a cathodic electrophoretic deposition process. Graphene oxide could promote the proliferation of cells by in vitro cytotoxicity tests [33]. This document got 218 total citations. Another study, "Nano Ag/ZnO-Incorporated Hydroxyapatite Composite Coatings: Highly Effective Infection Prevention and Excellent Osteointegration," 2018 used metals as an additive material. Argentum (Ag) and zirconia oxide (ZnO) nanoparticles were mixed with hydroxyapatite to coat Ti6Al4V discs by laser cladding. The samples showed good antibacterial activity on *Escherichia coli* and *Staphylococcus aureus*. After in vivo testing on rabbit femoral, the composite coating rapidly formation of new tissues [34].

Besides materials, several methods for producing titanium hydroxyapatite composite became the keywords that researchers in result data often use. A process of implant materials for biomedical applications is shown in Figure 8. "Composite coatings" is a more significant density than other processes keywords. The composite coating is widely used for biomedical because of its function in lifespan implant materials. To repair or replace tissue bones, implant materials are expected to promote cell proliferation. Implant materials for orthopedic and dental generally are metal materials, such as titanium, stainless steel, and cobalt-based alloys. The coating on metal implant materials could improve corrosion resistance [35].

Figure 8 contains some keywords about methods to synthesize composite coatings. Electrophoresis, electrophoretic coating, and plasma spraying coatings are some examples. A document from Li, Ming; Liu, Qian; Jia, Zhaojun; Xu, Xuchen; Cheng, Yan;

Zheng, Yufeng; Xi, Tingfei; and Wei, Shicheng discussed the electrophoretic process of coating titanium substrate using graphene oxide and hydroxyapatite composite. Titanium substrate soaked on GO/HA suspensions in a glass beaker with a voltage of 30V for 1–5 minutes using stainless steel as an anode and Ti substrate as a cathode 2 cm apart [33].

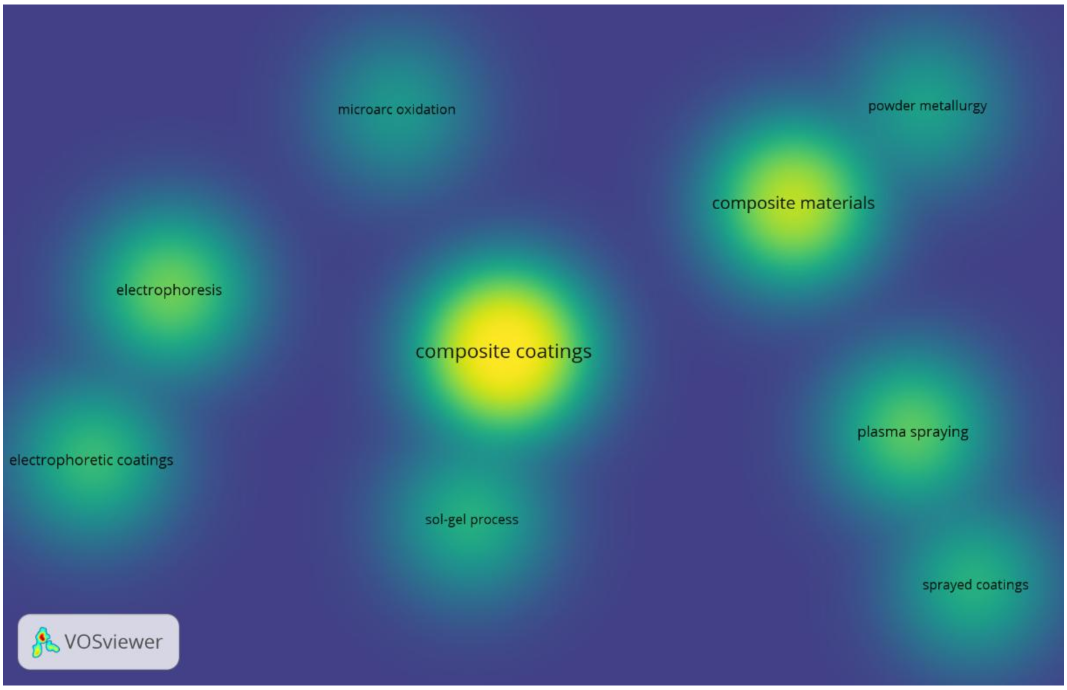


Figure 8. The process to produce titanium hydroxyapatite composite

Powder metallurgy is also a quite widely used method in Ti-HA composite. Fumio Watari, Atsuro Yokoyama, Mamuro Omori, Toshio Hirai, Hideomi Kondo, Motohiro Uo, and Takao Kawasaki conducted research to produce functionally graded materials (FGM) using hydroxyapatite/titanium by powder metallurgy method to optimize mechanical properties and biocompatibility. The process started with a mixture of powders, compressing, and sintering. Functionally graded material (FGM) Ti/HA has the efficient osteogenesis ability of biocompatibility and mechanical properties for implant materials [36].

4. Conclusion

Research about titanium hydroxyapatite composite as an implant material is a topic that many researchers worldwide have a low modulus elasticity, corrosion resistance, and biocompatibility from hydroxyapatite which enhances the bioactive properties of bone graft. Publications in the form of research articles and article reviews regarding the methodology for producing composites, various additives materials, and results of mechanical testing, in vitro and in vivo testing on animals have been widely carried out. This study has been conducting a bibliometric analysis of 932 articles and reviews documents. The document collected from the SCOPUS database for the limitation time from 2000 until June 4th, 2022 with the Materials Science and Engineering as subject areas. All documents are in the English language. Visualization of the documents was carried out using VOS-viewer and Biblio-shiny software. China became the top total publication country with 232 papers.

Meanwhile, the United States got a total citation of 8,536 cited documents and a total publication of 56. The total citations were followed by China, Japan, Iran, and India. Sichuan University, China became the top affiliation with 99 contribution authors, and Nanyang Technological University, Singapore, with 51 authors. Biomaterials, as a top 15 source of publication, has published a total of 34 documents with total citations of 10,834. Biomaterials have the highest h-index with 32, thus significantly impacting research in the Ti-HA composite field. A document by Karageorgiu, V. in 2005, published in Biomaterials, got a total citation of 4,563 documents, and a document by Kokubo, T. in 2003 got a total citation of 1,600. Materials Science and Engineering C got total citations of 2,071 documents, with an h-index of 30. Khor, K.A.; Khalil-Alafi, J; and Basu, B. were the top three authors with total published articles in this field, 15, 14, and 12 documents, respectively. The main topics from the authors' keywords are “hydroxyapatite” and “composite coatings.” Research related to titanium hydroxyapatite composite has prospects for further development to be used as an implant material in biomedical applications.

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