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AN OVERVIEW OF SCIENTIFIC PRODUCTION ON INJECTABLE ANTINEOPLASTICS IN THE WEB OF SCIENCE DATABASE AS A CONTRIBUTION TO PUBLIC HEALTH MANAGEMENT

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Abstract

According to data from the United Nations, cancer is the second leading cause of death in the world. Studies in the area advocate that this data be treated in an agile manner, to extract essential information. This work analyzed the characteristics of the world's scientific production on injectable oncologic agents present in articles in the Web of Science database between 2001 and 2021. Bibliometrics were performed on 1,496 articles. There was a constant increase in publications over the years – emphasis on 2021. The technological domain “pharmacy and pharmacology” was the most recurrent. China is the leader with a total of 505, while Elsevier was the publisher of the most published articles in the analyzed period. In relation to the most productive authors, Qian ZY stands out, with 18 articles. The most productive institution is the Chinese Academy of Sciences with 68 articles. Concerning networks using VOSviewer®, the following stand out: Li, Y. et al. (2012), (co-citation of references; 62); “Biomaterials” (co-citation of journals; 3,006); nanoparticles (keyword co-occurrence; 262); Soo-Chang Song (bibliographic coupling; 776). The study helps public health stakeholders in injectable antineoplastics to obtain essential information and thus contribute to better health management in both the public and private sectors.

Keywords: bibliometric analysis, cancer, injectable antineoplastics, co-citation, public health

Introduction

According to data from the World Health Organization (WHO), in the last two decades, the total number of people diagnosed with cancer practically doubled, going from around 10 million in 2000 to 19.3 million in 2020. Studies also suggest that the number of people diagnosed with cancer will increase in the coming years (WHO, 2021). Neoplasms can occur

due to several factors, either due to exposure to external causes (environment) or internal causes (genetic mutations, hormones, and immunological conditions), or even the interaction of these two causes. Among the main factors that lead to the development of neoplasms are smoking, diet, obesity, alcohol, sedentary lifestyle, frequent contact with carcinogens, exposure to radiation, age, ethnicity and gender (Buono & Azevedo, 2017; Fortes & Novaes, 2006; Santos, 2018).

Cancer continues to be seen as a public health challenge, requiring a focus on disease prevention and control actions. With regard to the discovery of new drugs in the pharmaceutical industry, the total time for their development exceeds 10 years. In this way, the process of innovation in drugs and antineoplastic drugs needs to be constant, due to the need for new drugs to circumvent the process of resistance acquired by tumor cells, as well as the constant discovery of new metabolic routes that lead to the emergence and maintenance of activity of tumor cells (Al-Lazikani et al., 2012; Holohan et al., 2013).

Therapies available for the treatment of cancers include chemotherapeutic agents, biologics, molecular-targeted therapy, radiotherapy, surgery, and interventional oncology (Ramos et al., 2021; Sag et al., 2016). In the pharmaceutical area, the manipulation of injectable drugs is a complex activity, since they are not commercially available, making it possible to prepare them in a personalized way to solve the specific needs of the patient: individualization of the dose, addition of components to the formulation, choice of the type of diluent volume suitable for the clinical condition of the patient and adequacy of the formulation to the route of administration (“ASHP Guidelines on Compounding Sterile Preparations”, 2014; Mohiuddin, 2020; Pergolizzi Jr et al., 2013).

In the contemporary world scenario, science, technology and innovation (ST&I) are considered fundamental instruments for development, economic growth, job and income generation and democratization of opportunities (Pacti, 2010). Technological advances and information systems have led to advances in different areas of knowledge. As a result of these new technologies, information is obtained in real time, favoring a faster dissemination of knowledge. Concerning the health area, information systems have been increasingly used as tools to support the health of the population and in public health activities related to prevention and health promotion, disease control, surveillance and monitoring (Ball et al., 2009). In this way, it becomes urgent to evaluate the performance of scientific activity and its impact on society so that resources destined for Research and Development (R&D) can be appropriately allocated (Sancho, 1990).

In the paradigm of the information and knowledge society, the innovation society is the result. Therefore, access to scientific and up-to-date information is crucial for the scientific and technological development of a country. In this context, one can mention bibliometrics, one of the branches of scientometrics, which aims to assess, through quantitative techniques, scientific production in the various means of scientific communication (Cunha & Cavalcanti, 2008). The data for carrying out this work were collected from the Web of Science (WoS).

Due to the ease of access, databases have been increasingly used by researchers, specialists and managers, as they allow them to monitor the scientific production in their area, as well as share their research with the academic and scientific community. These databases allow the indexing of various types of documents (books, theses, dissertations, journals, annals of events, etc.), making it possible to recover and use scientific knowledge, search for bibliographic references, in addition to serving as indicators of the potential impact of a journal in a particular area of knowledge (Lacerda et al., 2012; Podsakoff et al., 2005). Among the various databases available on the Internet, there are Google Scholar, Scielo, Scopus (Elsevier), Pubmed (Medline) and Web of Science (ISI - Institute for Scientific Information). In this sense, it is possible to quantify the most productive authors, the emerging paradigms, the combination of disciplines and journals, which participate in the process of disseminating scientific knowledge (Ikpaahindi, 1985).

Bibliometric analyzes can be considered facilitating tools in the analysis of information stored in different databases, allowing researchers to obtain an overview of the scientific and technological level of a country or area of knowledge (Soares et al., 2016). In addition, these

analyzes can help decision makers to identify trends in the growth of knowledge in a given area, understand new themes, assess their local or global influence, identify possible gaps, determine the dispersion and obsolescence of scientific fields, point out authors and more productive institutions, verify the quality of research carried out in the area, as well as identify the journals most used in the dissemination of research results in a given field of knowledge (Figueredo et al., 2020; Quevedo-Silva et al., 2016; Soares et al., 2016).

Thus, the study demonstrates how information science can help in the management of innovation for Public Health in the area of injectable oncology, through the treatment of scientific data on cancer. In addition, it is intended to contribute to the management of public health policies, as well as to identify the world scenario in research and development of technology in injectable oncology for application in cancer therapy, considering the time span of 20 years.

Research Methodology

General Background

The study was considered descriptive. A document-based quali-quantitative approach, based on the Web of Science. Scientific production in the national and international scientific community was analyzed. In it, the most relevant articles and authors were identified, the scientific journals with the greatest coverage for the subject in vogue.

Procedures Background

Scientific production data based on articles and review articles published in journals indexed in the Web of Science database between 2001 and 2021 were used. To this end, the search terms “injectable AND (cancer OR tumor)” were used, with the filters “Title” and “Summary” in the search fields and the Boolean operator “OR”, linking these fields. Then the filters “Types of documents” were applied, in which the options “articles” and “review articles” were chosen. The data were exported from the Web of Science database so that they could then be processed using the VOSviewer® program, which allows you to create, visualize and explore bibliometric maps based on network data (van Eck & Waltman, 2010). This tool supports bibliometric studies and enables the mapping of scientific knowledge through international productions in databases such as Web of Science, Scopus and Pubmed. The results of the analyzes provide a panoramic view of the bibliometric data, as well as making it possible to identify gaps in current and future research (Peixe & Pinto, 2021). With the use of the software in question, co-citation analyzes of references, sources, co-occurrence of keywords (All Keywords) and bibliographic coupling of the articles analyzed were performed.

Research Results

Cancer is one of the main global public health problems. In the 21st century, although the number of cases of this disease grows alarmingly, scientific and technological studies are also advancing to understand tumors and therapy options that can make it a chronic disease. It is noted that deaths occur not only in aging populations, but also in children and adults who are in the most active period of their lives. This represents a tremendous public health issue that cannot be ignored by politicians or citizens alike. Fortunately, there is a growing awareness that while cancer is a problem for doctors to address, it should also be a concern for researchers, policy makers, business and civil society representatives who share their knowledge and interests, as well as their concerns. and experiences (*New Trends in Cancer for the 21st Century* | SpringerLink, 2006). Regarding treatment advances, those based on genetic sequencing and immunotherapy are presented – these are the best to contain the damage of the

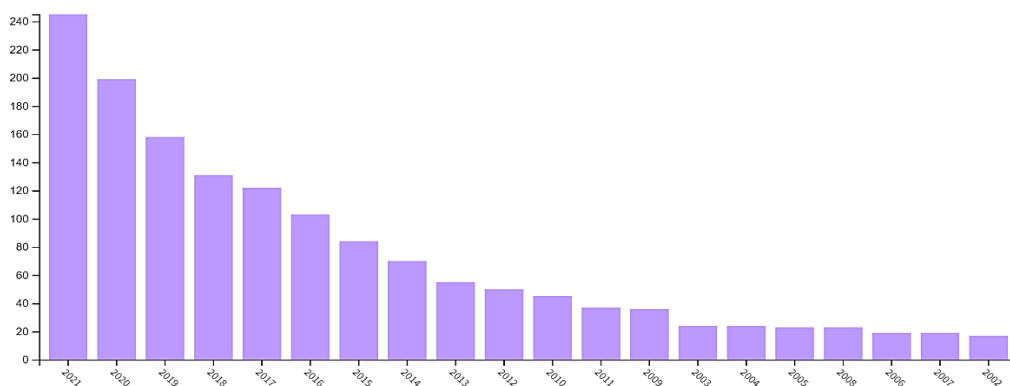
disease that could affect 27 million people by 2030. In Brazil, 704 thousand new cases of cancer are expected for each year of the triennium 2023-2025 (INCA, 2022).

With this scenario, the use of information science, through bibliometrics, can contribute to the identification of senior specialists in each area, as well as advances in research and more effective treatments in the world. The use of statistical and mathematical methods to analyze and build indicators on the dynamics and evolution of medical, scientific and technological information, assists in decision-making and the formulation of consistent public policies (Lima de Magalhaes et al., 2015).

Thus, to have an overview of the scientific production in injectable antineoplastic agents over the last 20 years, the search terms and filters described in the methodology were used.

A total of 1,496 articles on injectable antineoplastics were found in the WoS database from 2001 to 2021. A constant increase in the number of publications with the theme in question is observed in the period, revealing the interest in this public health issue. The largest number of indexed articles was in the year 2021, with 245 publications (16.38% of the total) (Figure 1).

Figure 1
Distribution of the Number of Articles Published in WoS between 2001 and 2021

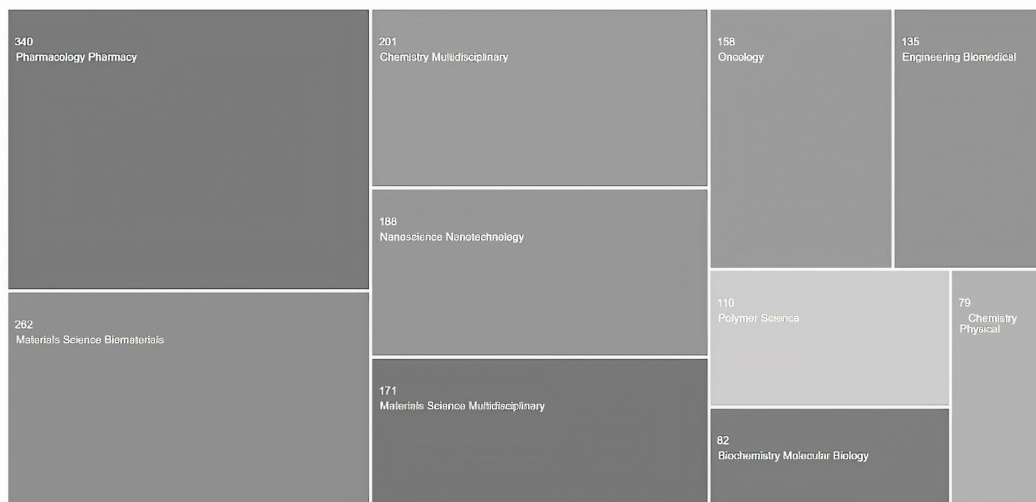


Source: Web of Science, 2022.

Figure 2 presents the Treemap type graph (tree map) showing the ten main health categories, listed and extracted from the WoS, where these articles are found. In this chart, the entire sample is divided into rectangles whose sizes are proportional to the number of articles viewed in each WoS category. As can be seen in the graph, most of the articles retrieved are in the category “pharmacy and pharmacology”, with a total of 340 articles (22.73%). Next, the following categories stand out: “material science biomaterials” with 262 (17.51%), “multidisciplinary chemistry” with 201 (13.44%), “nanoscience and nanotechnology” with 188 (12.57%), “science of multidisciplinary materials” with 171 (11.43%), “oncology” with 158 (10.56%), “biomedical engineering” with 135 (9.02%), “polymer science” with 110 (7.35%), “molecular biology biochemistry” with 82 (5.48%) and “physical chemistry” with 79 (5.28%). It should be noted that these categories are inserted in the complex framework of the Health area.

Despite of the ten main health categories of the total presented in the tree map (Figure 2), the largest proportion of articles corresponded to “pharmacy, pharmacology” (22.73%) and the smallest to “biochemistry, molecular biology” and “physical- chemistry” (5.48% and 5.28% respectively).

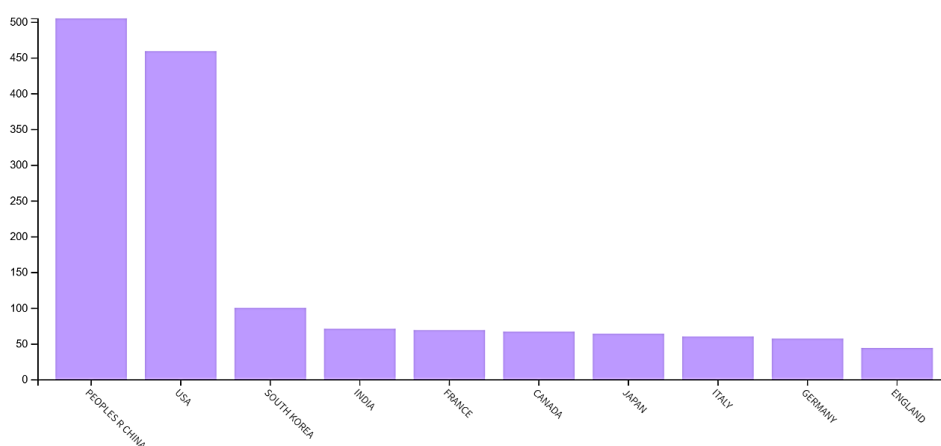
Figure 2
Tree Map of Top 10 WoS Categories Found in Articles Published between 2001 and 2021



Source: Web of Science, 2022.

In relation to the 10 most prolific countries (Figure 3). China leads the number of articles published with a total of 505 (33.76%), followed by the USA with 459 (30.68%), South Korea with 100 (6.68%), India with 71 (4.75%), France with 69 (4.61%), Canada with 67 (4.48%), Japan with 64 (4.28%), Italy with 60 (4.01%), Germany with 57 (3.81%) and England with 44 (2.94%).

Figure 3
Distribution of the Number of Articles Published in WoS among the top 10 Countries between 2001 and 2021



Source: Web of Science, 2022.

The ten publishers with the highest number of indexed articles (1,496) in descending order were: Elsevier with a total of 4,123 (27.54%), followed by the American Chemical Society publishers with 155 (10.29%), Wiley with 154 (10.29%), Springer Nature with 149 (9.96%), Royal Society of Chemistry with 112 (7.49%), Taylor & Francis with 69 (4.61%), Mdpi with 35 (2.34%), Lippincott Williams and Wilkins with 32 (2.14%), Sage with 31 (2.07%) and Dove Medical Press Ltd with 22 (1.47%).

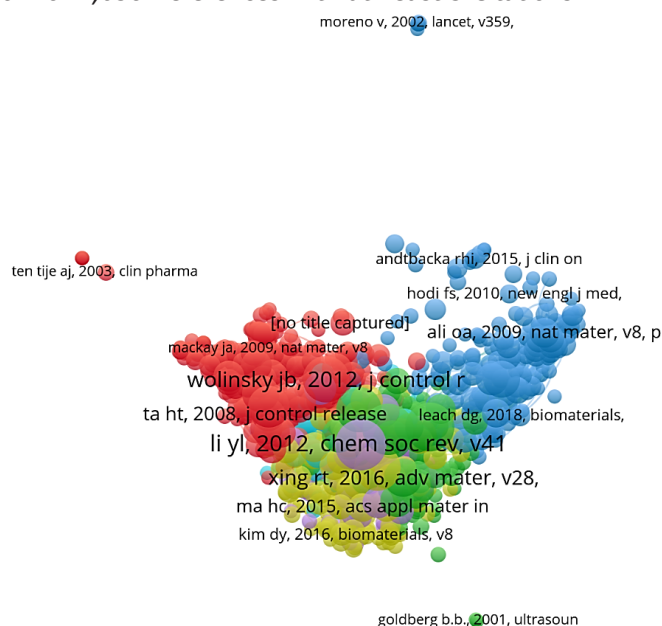
Regarding the most productive authors in Public Health for injectable antineoplastics, found in the analyzed articles, the author Qian ZY stands out, appearing in 18 articles (1.20%). Following, stand out the authors Zhang J, with 17 articles (1.17%); Chen Y and Wang HX with 16 (1.07%); Li J, Song SC and Zhang Y with 15 (1.00%); Wang WW with 14 (0.94%) and Dong AJ and Zhou L with 13 (0.87%).

Among the institutions that most published review articles in the analyzed period, the Chinese Academy of Sciences stands out with a total of 68 (4.14%), followed by Sichuan University with 50 (3.34%), University of California System with 49 (3.28%), University of Texas System with 37 (2.47%), Udice French Research Universities with 36 (12.41%), Harvard University with 35 (2.34%), Zhejiang University with 34 (2.27%), Chinese Academy of Medical Sciences Peking Union Medical College and Duke University with 26 (1.74%) and University of California Los Angeles with 25 (1.67%).

About the co-citation analyzes of the references and sources present in the retrieved articles, the VOSViewer® program was used to process these data. This type of analysis measures the relationship between two articles based on the number of publications in which they appear cited simultaneously (Grácio, 2016). The greater the number of co-citations, the greater the relationship between cited authors. In this way, the co-citation graph obtained will indicate how knowledge in a given area is perceived by researchers present in the journals analyzed (Grácio, 2013).

Figure 4 presents the co-citation network of references extracted from the 1,496 WO documents, which highlights the references shared by the authors of the documents. In the network formed, the largest nodes and names of references show their greatest occurrence. The different colors present in the network indicate the groupings in clusters and the lines show the interrelationship of these references. Clusters are groups that form due to affinity or proximity, identifying the strongest relationships within the group as a whole. Of the 56,277 references cited, 1,058 have at least 5 citations. In the fifth largest cluster, identified in the graph in red, the reference with the highest number of co-citations (62) identified is: Li, Y., Rodrigues, J., & Tomás, H. (2012). Injectable and biodegradable hydrogels: gelation, biodegradation and biomedical applications. *Chemical Society Reviews*, 41(6), 2193–2221. Doi:10.1039/c1cs15203c.

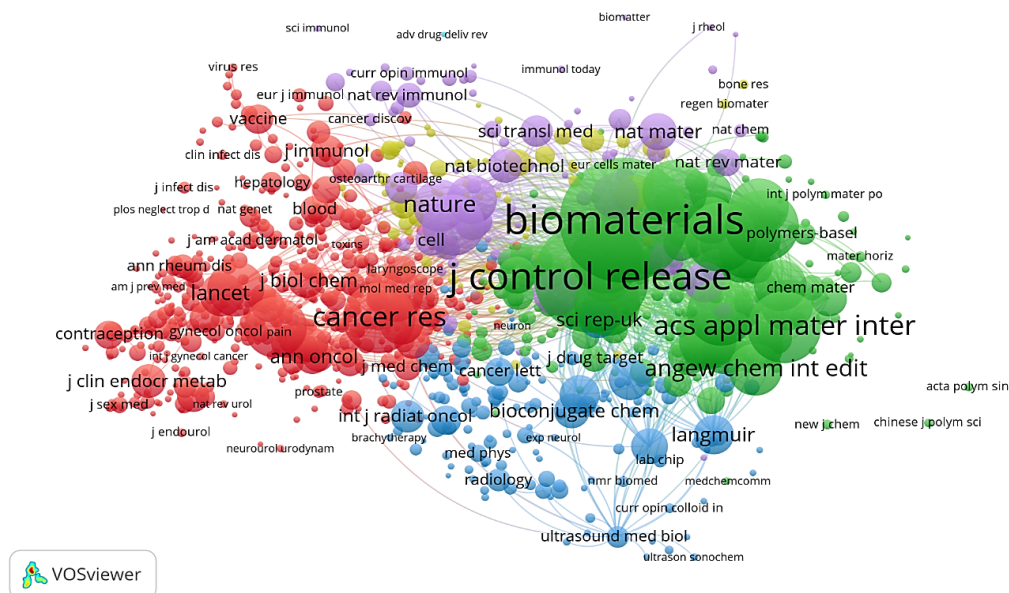
Figure 4
Co-citation Network of 1,058 References with at Least 5 Citations



Source: Created by the authors using VOSViewer®, 2022.

By analyzing the articles imported from WoS and the references used in the journals, it was possible to create a co-citation map with VOSViewer® of the most relevant journals for the area of Public Health in injectable antineoplastics (Figure 5). This type of analysis is very useful for specialists or managers who work with certain themes, as it can help them to choose the most interesting and reliable sources for the development of their projects. Of the 7,062 cited journals, 1,064 have at least eight citations. This chart shows that there are six main groups of publication sources for user studies on the subject. The most cited journal is “Biomaterials” (3,006 citations), followed by “Journal of Controlled Release” (2,443 citations) and “Advanced Materials” (995 citations). These three journals are part of the second largest cluster on the map (205 journals), represented in green. The largest cluster appears represented in red in the graph, containing 530 journals.

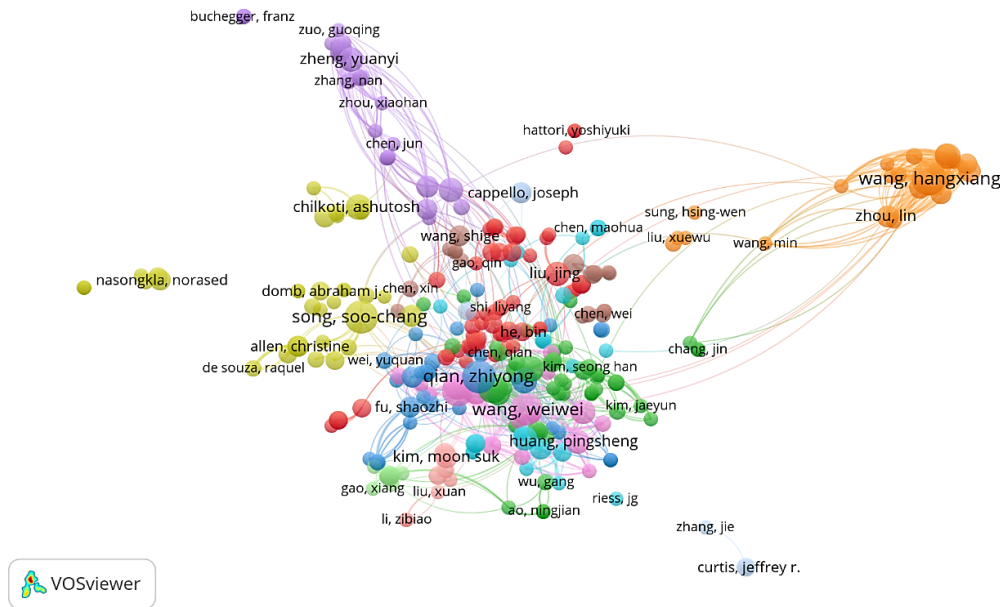
Figure 5
Co-citation Network of 296 Sources with at Least 3 Citations



Source: Created by the authors using VOSViewer®, 2022.

Figure 6 shows the network of co-occurrences of the 1,004 keywords (All Keywords). Of the total of 7,183 keywords resulting from the search, 1,004 keywords had at least three occurrences (extracted from the title, abstract and list of keywords), forming 15 clusters. The three most frequent keywords were nanoparticles (262), located in the ninth largest cluster, identified in the graph in pink; word cancer (221) located in the largest cluster of the graph, identified in the graph in red. In third place, the word drug-delivery (214) stands out, located in the eleventh largest cluster, identified in the graph in light green. There is a predominance of studies involving the use of nanoparticles for the treatment of various types of cancer. Research using nanoparticles opens up new fields of study, which result in countless opportunities for application in humans. With regard to forms of cancer treatment, nanoparticles can act in two ways: i) active, through the use of ligands or antibodies on their surfaces that bind to certain cells; ii) passive, in which the particles accumulate in the tumor tissues due to the wide fenestrations of the tumor endothelium (Carvalho Lopes & Pereira Torres, 2020).

Figure 7
Bibliographic Linking Network of 376 Authors with at Least 3 Documents and 3 Citations in the WoS Database



Source: Created by the authors using VOSViewer®, 2022.

Conclusions and Implications

The present work sought, through the measurement of scientific productivity, to estimate the magnitude of the theme of Public Health, “injectable oncologicals” and, for that purpose, it used bibliometric analyzes in the WoS database. The results showed that the theme has a scientific maturation in the area, evidenced by the number of published articles and globally involved researchers.

Through the analysis of articles and journals, it was possible to establish the most relevant authors, countries, publishers, and institutions for the area of Public Health in injectable antineoplastics. Of the 1,496 articles extracted from WoS between 2001 and 2021, there was a constant increase in the number of publications over the years, with emphasis on the year 2021 (245 publications). With the search terms used in WoS, it was observed that most of the extracted articles are in the category “pharmacy pharmacology” (340 articles).

China leads the number of published articles (505), while Elsevier was the publisher that most published Public Health articles in the area in question and in the analyzed period (4,123 articles). Among the analyzed institutions, the Chinese Academy of Sciences deserves mention, with a total of 68 articles published. In relation to the most productive authors, author Qian ZY stands out, appearing in 18 articles.

The mapping of publications through clusters, generated through the VOSViewer® software, constitutes a contribution to the rapid identification of potential networks and strong groups in the area, since the graphics generated by the program allow data mining, with subsequent recomposition information in order to stratify authors, sources, references and keywords linked to publications in their various contexts.

The use of information science to assist in the 'mining of identified data' and, therefore, to obtain essential information for decision-making in the area of Public Health, is presented as an advantage in the ease of obtaining quick adjustments, open data control in effective reproduction, as well as the reduction of time in the analysis. In this way, the analyzes made by program and/or software can contribute to the improvement in the process of dissemination and transparency of information, evidenced through the reports, as well as pointing out the most relevant documents from the different areas of science to be used in the development of research in the area.

The co-citation analysis of the bibliographic references showed that the most co-cited reference was Li, Y. et al. (2012), presenting a total of 62 co-citations. The journal co-citation analyzes showed that the most co-cited journal is "Biomaterials" (3,006 citations) and the keyword with the highest co-occurrence was nanoparticles (262). Regarding the bibliographic coupling, the author Soo-Chang Song (song, soo-chang), appears as the most prolific of all the authors in the formed network, centralizing the relationships in the fourth largest cluster.

Thus, it can be inferred that the results obtained with the bibliometric analyzes evidenced the important role of scientific productions in the area of Public Health, involving injectable oncologic agents in the scientific community. The theme expanded over the years, as well as consistency in the formation of production networks and collaboration between authors. Understanding the state of the art of studies on injectable oncology is essential in the health area, as it helps the scientific community and public and private agencies to assess the gaps that still exist, as well as to identify research trends in this field of knowledge. It is hoped that the present study can guide future works in the area, helping readers, researchers or health managers to identify the main scientific productions and thematic focuses in the area, thus subsidizing the discovery of new treatments or medicines for the different types of cancers.

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Declaration of Interest

The authors declare no competing interest.

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