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ARTICLE

Research Developments Analysis on Gold Nanoparticles (AuNPS) as Antimicrobial Agents through Bibliometric Computational Mapping using VOSviewer

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Diterima 01 Mar 2023
Diperbaiki 28 Mar 2023
Diterbitkan 15 Apr 2023

ABSTRACT

The many uses of gold nanoparticles in the biomedical field, including as an antimicrobial agent, prompted us to analyze the development of gold nanoparticles as antimicrobial agents research through a bibliometric approach with computational mapping analysis. The publication data used are publications from the Google Scholar database using the Publish or Perish Reference Manager software. The article's title, abstract, and publication year are used as a reference in processing publication data to make it more relevant and specific to the related topic, and the data is visualized by VOSviewer software. Found 257 highly relevant publication articles on related issues indexed by Google Scholar during the last ten years (2013 to 2022). The results show that research on associated topics has developed well because the number of publications has not decreased from 2013-2021, and until August 2022, the number of publications reached an amount equivalent to the number of publications in 2015-2017. The bibliometric results show that the publication trend of gold nanoparticles as antimicrobial agents is directed at studies on antimicrobial effect, antimicrobial property, and antiviral activity. The results of this study are expected to be used as a first step for further research on related topics.

Keywords: Bibliometric; Computational: Gold nanoparticles; Antimicrobial; and Vosviewer.

INTRODUCTION

Nanoparticles are suitable candidates in various commercial and domestic applications, especially in medical applications. This is because nanoparticles have high surface area due to their nanoscale size [1]. Nanoparticles such as gold, silver, copper, and zinc oxide are commonly used in medical and pharmaceutical applications as antibacterial, antifungal, antiviral, anticancer, and anti-inflammatory agents [2].

According to Ashraf, et al. (2016), gold nanoparticles are considered one of the most commonly used metals for biomedical applications due to their unique properties, such as the shape, size, and surface characteristics of gold nanoparticles that can be modified. In addition, gold nanoparticles have good biocompatibility, strong adsorption ability, low cytotoxicity, multifunctional potential, and high stability [3-4].

Gold in the form of nanoparticles (AuNPS) has been widely studied for its biological activity as an antimicrobial, including antifungal, antibacterial, and antiviral [5–8]. According to its antimicrobial properties, gold nanoparticles adhere to the surface of microbial cells. This interaction causes structural changes and damage to cells, ultimately leading to cell death. Therefore, gold nanoparticles are harmful to microbes, especially bacteria and fungi. Gold nanoparticles bind tightly to the surface of microorganisms, causing cell damage indicated by the destruction of flagella [9]. The results of research conducted by Zawrah, et al. [9], proved that drugs coated with gold nanoparticles had higher antimicrobial activity than pure drugs. The presence of gold nanoparticles in the drug makes it more effective against Gram-negative bacteria due to the thin peptidoglycan layer on the bacteria cell wall. Thus, the use of medicines coated with gold nanoparticles can minimize the length of treatment and side effects of the drug.

The high human demand for antimicrobials in various applications has increased the development of gold nanoparticles as research antimicrobial agents. However, in the field of study, the development of this research cannot be ascertained whether this research is still in great demand or not. For this reason, we use bibliometric analysis techniques to answer this question.

Bibliometric analysis is a popular and rigorous method for exploring and analyzing large amounts of scientific data related to citations, including keywords, authors, journals, countries, etc. [10]. Bibliometric analysis is also defined as a meta-analysis of research data that can assist researchers in studying bibliographic content and citation analysis of an article published in a journal or other scientific work [11]. Recently, there have been many studies on bibliometric analysis in the scope of chemistry, including nanoparticles, such as magnetite nanoparticles [12-13], nanoparticle toxicity [14–16], silver nanoparticles [17], synthesized nanoparticles [18-19], magnetic nanoparticles [20-21].

However, from several research data on bibliometric analysis of nanoparticles that have been published, there has been no research discussing the development of gold nanoparticles as antimicrobial agent research. In particular, bibliometric analysis for research in the last ten years, from 2013 to 2022, through the VOSviewer software. Therefore, this study was conducted to analyze the development of gold nanoparticle research as an antimicrobial agent with a bibliometric approach to articles indexed by Google Scholar using VOSviewer software. This research was conducted with the hope that it can be the first step for researchers in conducting and determining research themes, especially those related to gold nanoparticles as antimicrobial agents.

METHOD

The publication data used in this study are based on articles published in journals indexed by Google Scholar. The Publish or Perish Reference Manager software was used to conduct a literature review and obtain research data on gold nanoparticles as an antimicrobial agent. Visualization of the results of bibliometric analysis using the VOSviewer software. This research method is carried out through several stages, described in the following subsections.

2.1 Bibliometric Analysis Database

The first step in conducting a bibliometric analysis is to decide on an appropriate database to obtain research data relevant to the chosen topic [22]. This study used the Google Scholar database to fulfil the research objectives. Google Scholar is an open-source database. We developed a specific search to collect several publications in the form of potential journals using the Publish or Perish Reference Manager software that focuses on three aspects, such as research titles with the search form using an OR query, namely "Gold Nanoparticles OR AuNP OR AuNPS", year of publication in the last ten years (2013-2022), and keywords with the search form using OR and NOT queries, namely "antimicrobial OR antibacterial OR antifungal OR antiviral NOT antioxidant NOT anticancer". Search queries were made narrower and more specific to ensure that the data obtained were relevant to the research topic.

2.2 Data Analysis Methods

The results of collecting publication data in the Publish or Perish Reference Manager application are further processed using Microsoft Excel software. Before the data is processed in the software, the results of the published data collection in the Publish or Perish application are further filtered so that the data collected is relevant to the research topic, with the following criteria.

1. Each article must include the words "Gold Nanoparticles" at least in the title. In addition, articles that have the comments "Antimicrobial", "Antibacterial", "Antifungal", or "Antiviral" are considered more relevant to the research topic.
2. If point 1 is not met, then at least the article should include the word "Gold Nanoparticle" and discuss antimicrobial, antibacterial, antifungal, or antiviral activity in the abstract.
3. The article includes the year of publication from 2013 to 2022.

The articles that have been collected and meet the criteria for the analysis of this research are then exported into two types of files: research information system (.ris) and comma-separated value format (*.csv). The data set is then further processed in the Microsoft Excel application.

2.3 Bilbiometric Computational Mapping

Bibliometric mapping was performed using VOSviewer software. VOSviewer is also used to visualize and evaluate trends using bibliometric maps. The article data from the source database is then mapped. VOSviewer is used to create three mapping publications variations: network visualization, density visualization, and network-based overlay visualization (co-citation) between existing items. When creating a bibliometric map, the keyword occurrences are set to be found at least three times. We removed the less relevant terms and keywords.

RESULTS AND DISCUSSION

3.1. Data Search Results and Analysis of Publication Development

Based on the search for publication data through the Publish or Perish Reference Manager application from the Google Scholar database, we obtained 711 publication articles. Of the 711 published articles obtained, 257 publication articles are very relevant to the selected criteria after going through the article data processing process. According to Rogers et al. (2020), it should be noted that to fulfil the bibliometric analysis, the data generated must consist of at least 200 articles [23]. From that, the data

collection results in this study are considered acceptable and meet the requirements of bibliometric analysis. The data from research metadata consists of the author's name, title, year, journal name, publisher, number of citations, article links, and related URLs.

Table 1 shows the development of research on Gold Nanoparticles as Antimicrobial Agents published in Google Scholar indexed journals. Based on the data in Table 1, we can see that the number of researches on Gold Nanoparticles as Antimicrobial Agents is 257 articles from 2013-2022. In 2013 there were 14 articles, followed by 20 articles in 2014, 24 articles in 2015-2017, 26 articles in 2018-2019, 35 articles in 2020, 40 articles in 2021, and 24 articles until July 2022. The number of publications shows that research on Gold Nanoparticles as Antimicrobial Agents is growing well every year, especially in the last ten years (2013-August 2022).

Table 1. The number of Related Publications Indexed by Google Scholar per Year

Publication Year	Publication Number
2013	14
2014	20
2015	24
2016	24
2017	24
2018	26
2019	26
2020	35
2021	40
2022	24
TOTAL	**257**

The graph visualizes the number of annual publication data indexed by Google Scholar in Figure 1. As shown in Figure 1, research on gold nanoparticles as an antimicrobial agent is considered well-developed and consistent. Publication growth did not decline from 2013-2021 and experienced only one less significant decline in 2022 in July. This decrease is because 2022 is not over yet, and it is still possible for researchers to conduct related research this year. The highest number of publications was recorded in 2021, with 40 articles (15.56% of the total publications), while 2013 was the least with 14 articles (5.44%).

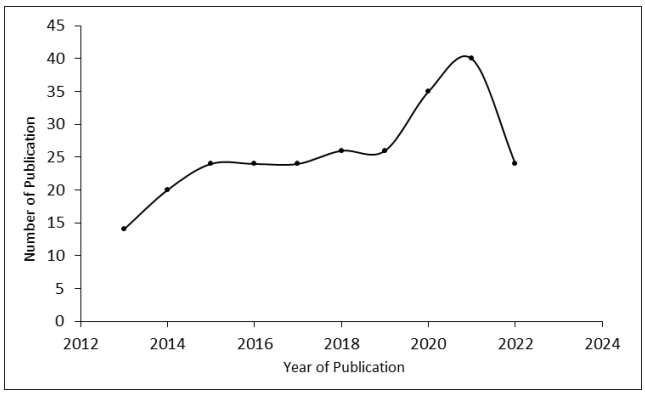

Figure 1. Google Scholar indexed Annual Publication Data

These data indirectly indicate that the publication of gold nanoparticles as an antimicrobial agent has promising prospects in the years to come because the publication number does not decrease every year. Even as of August 2022, publications on related topics have reached 24 articles, as in 2015-2017.

Table 2 shows examples of published data used in the VOSviewer analysis of this study. The data samples were the 20 best articles with the highest citations. The number of citations from 257 articles used in this study is 4886, the number of citations per year is 542,89, and the number of citations per article is 19.01.

Table 2. Publication of Gold Nanoparticles as Antimicrobial Agents with the Most Citation

No.	Title	Years	Total Cites	Cites/year	Ref
1.	Gold nanoparticles: an efficient antimicrobial agent against enteric bacterial human pathogen	2016	249	41.5	[24]
2.	Antibacterial effect of gold nanoparticles against *Corynebacterium pseudotuberculosis*	2017	171	34.2	[7]
3.	Synergy of non-antibiotic drugs and pyrimidinethiol on gold nanoparticles against superbugs	2013	159	17.67	[25]
4.	Eco-friendly synthesis and characterization of gold nanoparticles using *Klebsiella pneumoniae*	2013	105	11.67	[26]
5.	Silver and gold nanoparticles synthesized from *Streptomyces sp.* isolated from acid forest soil with special reference to its antibacterial activity against pathogens	2017	103	20.6	[27]

No.	Title	Years	Total Cites	Cites/year	Ref
6.	Photothermal killing of *Staphylococcus aureus* using antibody-targeted gold nanoparticles	2015	94	13.43	[28]
7.	Intracellular transport of silver and gold nanoparticles and biological responses: An update	2018	90	22.5	[29]
8.	Porous gold nanoparticles for attenuating infectivity of influenza A virus	2020	86	43	[30]
9.	Delivery of antiviral small interfering RNA with gold nanoparticles inhibits dengue virus infection in vitro	2014	82	10.25	[31]
10.	Kolanut (*Cola nitida*) mediated synthesis of silver–gold alloy nanoparticles: antifungal, catalytic, larvicidal, and thrombolytic applications	2016	74	12.33	[32]
11.	Interactions of gold and silver nanoparticles with bacterial biofilms: Molecular interactions behind inhibition and resistance	2020	68	34	[33]
12.	Antimicrobial and catalytic activities of biosynthesized gold, silver, and palladium nanoparticles from *Solanum nigrum* leaves	2020	67	33.5	[34]
13.	Phytosynthesis, characterization and fungicidal potential of emerging gold nanoparticles using *Pongamia pinnata* leaves extract: a novel approach in nanoparticle	2020	66	33	[35]
14.	Formulation of carbapenems loaded gold nanoparticles to combat multi-antibiotic bacterial resistance: In vitro antibacterial study	2017	64	12.8	[36]
15.	Morphological analysis of the antimicrobial action of silver and gold nanoparticles stabilized with ceftriaxone on *Escherichia coli* using atomic force microscopy	2014	55	6.88	[37]
16.	Controlled synthesis of gold nanoparticles *using Aspergillus terreus* IF0 and its antibacterial potential against Gram-negative pathogenic bacteria	2014	50	6.25	[38]
17.	Synthesis of silver and gold nanoparticles using cashew nut shell liquid and its antibacterial activity against fish pathogens	2014	49	6.13	[39]
18.	Endogenic mediated synthesis of gold nanoparticles bearing bactericidal activity	2016	49	8.17	[40]
19.	Antiviral activity of algae biosynthesized silver and gold nanoparticles against Herps Simplex (HSV-1) virus in vitro using cell-line culture technique	2022	49	49	[41]
20.	Antibacterial efficacy of gold and silver nanoparticles functionalized with the ubiquicidin (29–41) antimicrobial peptide	2017	41	8.2	[42]

The list of articles with the most citations are dominated by articles published in 2014, 2017, and 2020 (Table 2). The results of the study in Table 2 show that the article of Shamaila et al. (2016) on Gold nanoparticles: an efficient antimicrobial agent against enteric bacterial human pathogens is the most cited article with a total of 249 citations. The most recent articles included in Table 2 are articles published by El-Sheekh, et al. (2022). The article is the most cited article per year with 49 citations. In addition, 4 of the 20 articles with the most significant number of citations per year are still two years old. This data shows that the publication of gold nanoparticles as antimicrobial agents every year has active and positive development.

3.2. Visualization of Gold Nanoparticle Topic Area as Antimicrobial Agent using VOSviewer

After analyzing the published data using the Publish or Perish Reference Manager and processing the data further using Microsoft Excel, VOSviewer software analyzed the bibliometric results for computational mapping. Of the 104 keywords identified by VOSviewer from 257 publications, 62 met the threshold with a minimum of three occurrences, as shown in Figure 2.

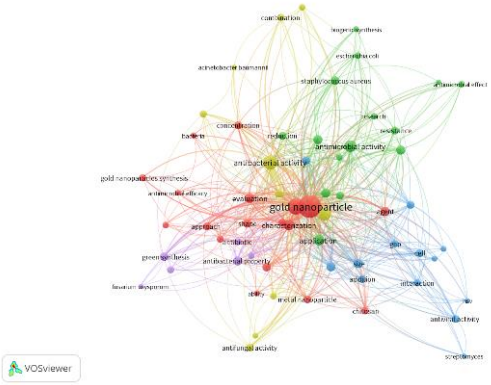

Figure 2. Network Visualization of Gold Nanoparticles as Antimicrobial Agent Research

As shown in Figure 2, five cluster themes of Gold Nanoparticles as Antimicrobial Agents were found. The first cluster marked in red has 18 items. The associations in Cluster 1 describe Gold nanoparticles in general, such as characterization, biosynthesis, ability, shape, surface, and mention of other terms such as AuNP, metal nanoparticles, and others. The second cluster in green has 15 items. This cluster investigates gold nanoparticles as antimicrobial agents, including their antimicrobial activity. The third cluster in blue has 13 items investigating Gold nanoparticles as antibacterial agents and their antiviral activity. The fourth yellow cluster with ten items investigated antibacterial and antifungal activity. Finally, the purple cluster has six items related to its antibacterial and antimicrobial properties, including antibiotics.

We should note that the results of network visualization on the keyword linkages found indicate that each cluster has a relationship with one another, so the linkage is still relevant between one cluster and another. In addition, in the results of the network visualization, Gold Nanoparticles, which have the largest circle with 227 occurrences, are related to all existing keywords, meaning that the 62 keywords we chose were relevant to Gold Nanoparticles. The occurrences of each keyword determine the size of this circle. The keyword antibacterial activity seems to be greater than antimicrobial agents because the publication of gold nanoparticles as antimicrobial agents is mainly done by researchers who focus on their antibacterial properties only. However, this is still acceptable considering that antibacterial is a topic that is still included in the scope of antimicrobials.

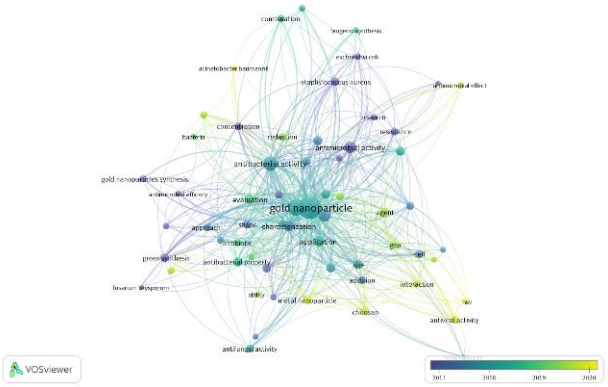

Figure 3. Overlay Visualization of Gold Nanoparticles as Antimicrobial Agents Research

The bibliometric results are also supported by the overlay visualization shown in Figure 3. The analysis results of this overlay visualization imply that Gold Nanoparticles are still a hot topic in publication. In Figure 3, Gold Nanoparticles are still widely discussed above the 2018 range as well as the primary focus as an antimicrobial agent. Even publications investigating the antimicrobial effect, antimicrobial property, and antiviral activity of Gold Nanoparticles have been widely studied since 2020. These data also support that the publication of Gold Nanoparticles as Antimicrobial Agents is very active and growing, considering that there are several publications with a high number of citations per year, owned by publications published since 2020.

Based on the analysis results of the collected article data, there are still many opportunities to implement the publication theme related to Gold Nanoparticles as Antimicrobial Agents in further research because the development of research on related topics is still active and consistent. In addition, the advantages of Gold Nanoparticles, which are widely used in various applications, also support researchers to investigate this material further, including as an antimicrobial agent. From the results of this study, we can find out the development of research on gold nanoparticles as antimicrobial agents

that are more specific, relevant, and rigorous as a first step in conducting further research.

CONCLUSION

Gold nanoparticles have a wide range of biomedical applications, including antimicrobial agents. A specific bibliometric analysis of the development of research on gold nanoparticles as antimicrobial agents in this paper was carried out for the first time. This research shows that related research continues to develop actively to enable researchers to take up this topic for research in the coming years. This active development is supported by the publication with the highest citations per year owned by four articles with a publication age of two years, and the number of publications per year does not decrease until 2021. Based on the bibliometric analysis, many studies of Gold nanoparticles as antimicrobials have been investigated through their antibacterial activity. In addition, the research direction of gold nanoparticles as an antimicrobial agent in the last two years is their antimicrobial effect, antimicrobial property, and antiviral activity. Research opportunities for gold nanoparticles are still vast, and related topics that have been discussed previously, we suggest to be explored further. Finally, the results of this study can support future researchers as the first step in a deeper understanding of publication trends with related topics.

AUTHOR'S CONTRIBUTION

ABDN understands and designs research and contributes methods. TMSE conducted the study, analyzed the data, and created the manuscript. All authors read and approved the final version of the manuscript.

ACKNOWLEDGMENT

We acknowledged Bangdos, Universitas Pendidikan Indonesia.

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