

Bibliometric Analysis of Nanomedicine Application in Parkinson's Disease using VOSviewer**Andre Safrie Maulana**Program Studi Kimia, Universitas Pendidikan Indonesia. Email: Andre.s.m@upi.edu**Abstract (English)**

Nanomedicine is a drug that has a size in the range of 1 – 100 nm. Nano-sized drugs can be applied as drug delivery agents by encapsulating or binding the active substance which then delivers the active substance to controlled tissue. Parkinson's disease is a disease caused by the loss of dopaminergic cells in the midbrain, so the treatment of Parkinson's disease is to provide increased dopamine concentrations or stimulate dopamine receptors. This research aims to map research regarding the application of nanomedicine to Parkinson's disease from the aspects of researchers, publishers and citations. This research uses bibliometric analysis methods, the Publish or Perish search engine to search for data, and the VOSviewer application as a data mapping application. The time range used starts from 2017 to 2022, resulting in data for 284 articles. The results of this research found that the development of research regarding the application of nanomedicine to Parkinson's disease increases in publications every year, based on the highest number of citations with more than 100 citations consisting of 20 articles from various publisher sources. Meanwhile, in the co-occurrence analysis using VOSviewer, it was shown that in the network visualization the keywords that frequently appeared were "Parkinson", "field", and "Nanotechnology". In the overlay visualization the keywords "Parkinson's" and "nanomedicine" are not articles that discuss the most recent research. However, if you look at the topic density in "Nanomedicine" it is still small. This can help researchers determine the topic to be researched and can also be a reference for research related to the application of nanomedicine to Parkinson's disease.

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Abstrak (Indonesia)

Nanomedicine merupakan obat yang memiliki ukuran pada kisaran 1 – 100 nm. Obat berukuran nano dapat diaplikasikan sebagai agen penghantaran obat dengan cara mengenkapsulasi atau mengikat zat aktif yang kemudian mengantarkan zat aktif tersebut ke jaringan yang dikontrol. Penyakit Parkinson merupakan penyakit yang disebabkan oleh hilangnya sel dopaminergik pada otak tengah, sehingga pengobatan penyakit Parkinson adalah dengan memberikan peningkatan konsentrasi dopamin atau merangsang reseptor dopamin. Penelitian ini bertujuan untuk memetakan penelitian mengenai penerapan nanomedis pada penyakit parkinson dari aspek peneliti, penerbit dan sitasi. Penelitian ini menggunakan metode analisis bibliometrik, mesin pencari Publish or Perish untuk pencarian data, dan aplikasi VOSviewer sebagai aplikasi pemetaan data. Rentang waktu yang digunakan mulai tahun 2017 hingga 2022 sehingga menghasilkan data sebanyak 284 artikel. Hasil penelitian ini menemukan bahwa perkembangan penelitian mengenai penerapan nanomedis pada penyakit parkinson mengalami peningkatan publikasi setiap tahunnya, berdasarkan jumlah sitasi terbanyak yaitu lebih dari 100 sitasi yang terdiri dari 20 artikel dari berbagai sumber penerbit. Sedangkan pada analisis co-occurrence menggunakan VOSviewer menunjukkan bahwa pada visualisasi jaringan kata kunci yang sering muncul adalah "Parkinson", "field", dan "Nanotechnology". Pada visualisasi overlay kata kunci "Parkinson" dan "nanomedicine" bukanlah

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artikel yang membahas tentang penelitian terbaru. Namun jika melihat kepadatan topik di "Nanomedicine" masih kecil.

Introduction

Nanomedicine was popularized in the late 1990s to describe the application of the emerging field of nanotechnology, which seeks to exploit the unique properties and behavior of structures at the nanometer scale (<1 micrometer in size), for human health. (Shanker et al., 2011). One of the advantages of Nanomedicine is that the nanoparticle size can be modified (Wahyuddin, 2020). Nanomedicine is a drug that has a size in the range of 1 – 100 nm. Nano-sized drugs can be applied as drug delivery agents by encapsulating or binding the active substance which then delivers the active substance to controlled tissue. With its nanoscale size, drugs can penetrate into the tissue system, making drug delivery more efficient, and ensuring the drug acts on the targeted cells (Dwiastuti & Yuliani, 2021). Nanomedicine can overcome problems with conventional technology, including killing cancer cells effectively, rapid diagnosis, rapid replacement of organs (skin, muscles, digestive organs and sensors). So the existence of Nanomedicine allows the development of disease treatment quickly, effectively and efficiently (Floridha et al., 2016).

Parkinson's disease is a neurodegenerative disease that is most commonly found in the elderly and rarely occurs under the age of 30 years. Symptoms of this disease can appear from the age of 40 years with a peak in the 6th decade. Parkinson's disease is a chronic neurodegenerative disease characterized by three main signs, namely slowness of movement (bradykinesia), muscle stiffness (rigidity), and tremor at rest (resting tremor). (Alia et al., 2021). Drugs to control the symptoms that arise due to Parkinson's disease vary from patient to patient so there is no one definite drug that is the choice (Dahodwala et al., 2017). However, the drugs most commonly used to control the symptoms of Parkinson's disease include Levodopa, dopamine agonists, cholinesterase inhibitors, antimuscarinic drugs, monoamine oxidase-B (MAO-B) inhibitors, and amantadine. (Haddad et al., 2018). Parkinson's disease is a disease caused by the loss of dopaminergic cells in the midbrain, so the treatment of PP is by increasing dopamine concentrations or stimulating dopamine receptors. (Kalia & Lang, 2015). The main goal of PP treatment is to improve quality of life, this can be achieved through treating motor and non-motor symptoms. Treatment may include pharmacological and non-pharmacological interventions to maximize clinical outcomes (DeMaagd & Philip, 2005). Examples of research on nanomedicine are presented in table 1.

Table 1 Some examples of nanomedicine research

No	Title	Objectives	Results	Reference
1	Delivering the power of nanomedicine to patients today	investment to support the clinical translation of promising nanomedicine formulations should increase, not decrease. As the EMA recently encouraged in its roadmap to 2025, we must create more unity through common knowledge centers connecting academia, industry, healthcare providers and	ETPN's review of achievements in nanomedicine serves to strengthen our efforts to further expand and grow the maturity of nanomedicine for global healthcare, accelerating the pace of transformation of its enormous potential into real medical breakthroughs.	(Germain et al., 2020)

- hopefully policymakers to reduce the fragmentation that currently exists in the landscape standardization bodies and regulators. We must also promote cross-technological innovation strategies, support the development of nanomedicine as a high-value, low-cost solution to address unmet medical needs and help the most promising innovative projects in the field reach clinics better and faster.
- 2 Nanomedicine: An effective tool in cancer therapy
- The focus of this review is to explore different types of NPs and their surface/chemical modifications and targeting ligand attachment to tailor their properties to facilitate targeted delivery to cancer sites in a controlled manner.
- This review discusses the advantages of polymeric, magnetic, gold, and mesoporous silica NPs in delivering chemotherapeutic agents compared to conventional dosage formulations along with their drawbacks/risks and possible solutions/alternatives. In this CUR success story, there is the fact that its bioavailability is too low. To overcome this problem, new formulations such as nanoCUR were developed. CUR nanoformulation is a therapeutic alternative in the new discovery phase, because it is non-toxic to other body cells. Regarding nanocarrier formulations for delivery of CUR, SLN, NLC, liposomes, LCN and macrocyclic host macromolecules reported interesting characteristics that need to be studied further to better
- (Aftab et al., 2018)
- 3 Curcumin's nanomedicine formulations for therapeutic application in neurological diseases
- As expected, specific differences in these new formulations may influence their efficacy, explaining why most clinical trials show conflicting results regarding the beneficial effects of CUR in brain diseases, especially in the treatment of AD. Therefore, we must understand how existing CUR nanomedicine formulations work, including the benefits and harms specifically in AD and other brain conditions. This literature review aims to summarize the general bioactivity of CUR in neurological disorders, how functional molecules are extracted, and the different types of nanoformulations available.
- (Salehi et al., 2020)

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| 4 | Personalized nanomedicine for CNS diseases | Safe, non-invasive, and targeted drug delivery to the brain using nanoparticles (NPs) is currently receiving much research attention. | understand their mechanism of action and effectiveness. Future research will need to test these CUR nanoformulations, as well as different combinations and formulations, in brain diseases. New efforts are needed to test new CUR nanomedicine formulations, with improved CUR bioavailability, in brain diseases. | (Kaushik et al., 2018) |
| 5 | Nanomedicine-based immunotherapy for central nervous system disorders | we focus on the efficacy of nanomedicines that utilize immunotherapy to combat CNS disorders. Additionally, we summarize in detail nanomedicine-based pathways for CNS diseases that aim to deliver drugs across the BBB by mimicking the actions of innate immunity. | Here, we highlight advances in advanced personalized nanomedicine for the treatment of CNS diseases (with a focus on dementia), associated challenges, possible solutions, and prospects for nano-based personalized medicine. Unique immune functions in the CNS provide novel target mechanisms for amelioration of CNS diseases. Recently, various therapeutic approaches have been applied to combat brain-related disorders, with moderate results. Among various therapeutic strategies, nanomedicine-based immunotherapy systems represent a new era that can provide benefits with promising pharmacokinetics. This approach exploits molecular and cellular targeting of CNS disorders to improve safety, efficacy, and specificity. | (Hanif et al., 2020) |

In general, the application of nanotechnology can effectively reduce the side effects of painkillers and reduce the development of tolerance, thereby increasing the efficiency of treatment. Different pain relievers can be loaded onto various nanocarriers, including natural, synthetic, and copolymer nanocarriers, for different medical interventions (Mendoza & Arruebo, 2020; Song et al., 2022). One of them is in the field of cancer, nanotechnology has the potential to increase the efficacy of therapy, create detection methods, and target various stages of cancer. The development of various nanomaterials and nanotechnology has made it possible to improve the area of cancer biomarkers with a high precision and sensibility that was not possible a few years ago. (Teles et al., 2018).

Studying the molecular genetics of Parkinson's Disease is an important first step in understanding this disease, as it increases our knowledge of the relationship between phenotype and genotype. Whether by unraveling the complete etiopathogenesis of this disease, uncovering new pathogenetic mechanisms, or leading to other exciting findings, future molecular genetic studies will likely drive major advances in our understanding of this debilitating neurodegenerative disorder in the near future (Funayama et al., 2023).

Many studies have studied the influence of nanotechnology, especially nanomedicine. However, there have been no previous bibliometric reviews discussing the treatment of Parkinson's disease using nanomedicine. Based on several previous studies on nanomedicine, this is shown in table 2 which explains the bibliometric review regarding the application of nanomedicine. So it is hoped that this bibliometric analysis can help research topic areas specifically for Parkinson's disease with better methods such as nanomedicine.

Table 2 Bibliometric articles on previous applications of nanomedicine

No	Title	Topic Discussion	Ref
1	Clinical applications of nanomedicine in cancer therapy	this discussion examines the role of the developed nanomedicines in improving current therapeutic regimens from both therapeutic and pharmacokinetic viewpoints.	(Norouzi et al., 2020)
2	Need for Expansion of Pharmacy Education Globally for the Growing Field of Nanomedicine	overviews nanomedicine education in selected pharmacy programs globally, discusses current regulatory challenges, and describes various approaches to incorporating nanomedicine science in pharmacy programs around the world.	(Barton et al., 2022)
3	Biomedical Imaging: Principles, Technologies, Clinical Aspects, Contrast Agent, Limitations and Future Trends in Nanomedicines	This review article presents key advanced imaging modalities that provide relevant information about a patient's health through real-time monitoring to establish an accurate diagnosis and potential treatment plan.	(Wallyn & Anton, 2019)
4	Global research trends of nanotechnology for pain management	In this study, we used a bibliometric approach to examine the research status and global trends of nanotechnology in relation to pain management.	(Zhu et al., 2023)

No	Title	Topic Discussion	Ref
5	Global trends in nanomedicine research on triple negative breast cancer: a bibliometric analysis	to investigate research trends in nanotechnology in Triple negative breast cancer and compare research contributions from different regions, institutions, and authors.	(Teles et al., 2018)

Method

This research aims to obtain an overview of the application of nanomedicine to Parkinson's disease using bibliometric analysis methods. This analysis uses the Publish or Perish search engine to include research published in the last five years (2017-2022) on the topic of nanomedicine and the keywords Parkinson's disease. Articles that have been collected and meet the requirements for analysis in this research are then stored in research information system (*.ris) format. This format is included in the VOSviewer software to create a visualization of trends in the form of a bibliometric map. This bibliometric map consists of network visualization, overlay visualization, and density visualization (Nandiyanto et al., 2023). Based on the three bibliometric maps, the relationship between titles and authors is explained so that data results are obtained such as research development per year, authors with the most research, relationships between authors and other authors, as well as titles and other titles.

Result and Discussion

Publication Trends

Based on an article search using software, the number of articles that met the criteria for this topic area was 284 articles. 2021 is the year that contributed the most articles, namely 63 articles (22.18%). Then followed by 2022 with the number of articles not far from 2021, namely 62 articles (21.83%). Meanwhile, the publications that contributed the least were in 2018 with 29 articles with a percentage of 10.21%. The remaining publications published in 2020, 2019, and 2017 were 51 (17.96%), 41 (14.44%), and 38 (13.38%), respectively.

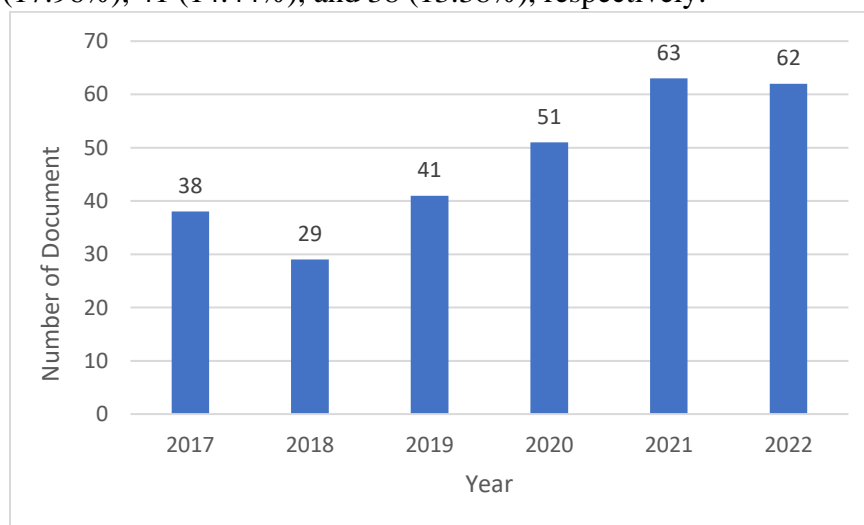


Figure 1. Number of documents published for the keywords “Nanomedicine” and “Parkinson's” between 2017 and 2022

Top Articles with Most Citations and Publisher

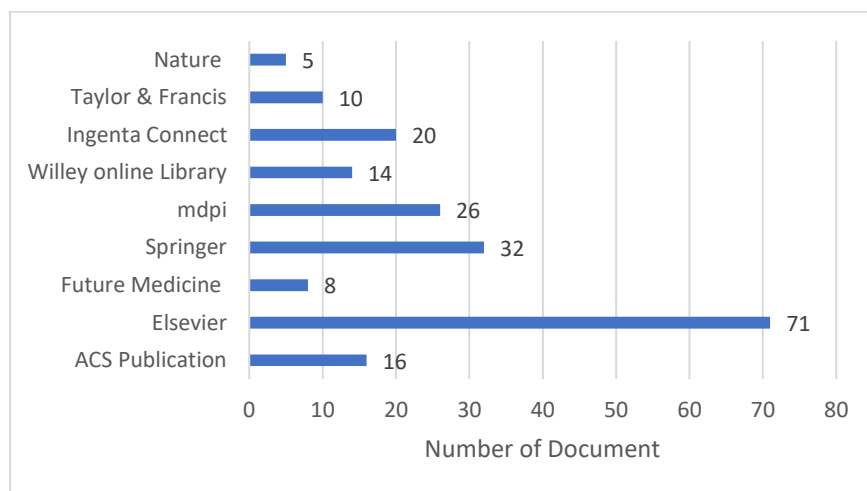
Bibliometric analysis based on the most citations has an important role because the more related citations there are, the more impact it has on society. However, this is not the only factor that can impact society. Other factors such as the methodology used, the content of the research, and contributions to the field may also influence the impact of this paper. This is presented in table 3 regarding the top 10 most quoted. The reference article that has the most citations is "Reactive oxygen species (ROS)-based nanomedicine" written by Yang et al. with 1346 citations. Apart from that, articles with citations above 100 consist of 20 related articles.

Table 3 Top 10 quotes on nanomedicine applications and parkinson's disease

No	Cites	Author	Title	Year	Journal Source	Publisher Source
1	1346	Yang et al.	Reactive oxygen species (ROS)-based nanomedicine	2019	Chemical Reviews	ACS Publications
2	913	Cabral et al.	Block copolymer micelles in nanomedicine applications	2018	Chemical Reviews	ACS Publications
3	589	Cheng et al.	Versatile polydopamine platforms: synthesis and promising applications for surface modification and advanced nanomedicine	2019	ACS Nano	ACS Publications
4	321	Peng et al.	Carbon dots: biomacromolecule interaction, bioimaging and nanomedicine	2017	Coordination Chemistry Reviews	Elsevier
5	286	Chen et al.	Black phosphorus nanosheets as a neuroprotective nanomedicine for neurodegenerative disorder therapy	2018	Advanced Materials	Wiley Online Library
6	233	Qiu et al.	Biocompatible and biodegradable inorganic nanostructures for nanomedicine: silicon and black phosphorus	2019	Nano Today	Elsevier
7	221	Germain et al.	Delivering the power of nanomedicine to patients today	2020	Journal of Controlled Release	Elsevier

8	189	Aftab et al.	Nanomedicine: An effective tool in cancer therapy	2018	International Journal of Pharmaceutics	Elsevier
9	187	Wu et al.	Extracellular vesicles: A bright star of nanomedicine	2021	Biomaterials	Elsevier
10	155	chan et al.	Biogreen synthesis of carbon dots for biotechnology and nanomedicine applications	2018	Nano-micro letters	Springer

Based on Figure 2, it shows the top 9 publishers based on the number of articles published by those publishers. In the top position is the publisher Elsevier with a total of 71 documents. Followed by the publisher Springer which has a total of 32 documents.



Figurer 1 Number of documents against the top 9 publisher sources

Co-Authorship Analysis of Autor

A visualization of the relationship between the author and other authors regarding the most active research in nanomedicine and Parkinson's disease is shown in the figure. In the analysis of this writing, there were a total of 73 who took part in related research out of a total of 824 authors. Based on the picture, there are 4 large clusters, namely cluster 1, which is shown in red, has 5 authors, cluster 2, which is marked in green, has 4 authors, cluster 3, which is shown in blue, has 2 authors, cluster 4, which is marked in color. yellow belongs to the same author as cluster 3, and others. It was previously mentioned that there were 73 authors who published about the application of nanomedicine, namely Xue Xue from Nankai University, China with 5 documents.

Based on Figure 3, there is a circle shape with different sizes for each circle. This explains the large number of related articles written by certain authors. The relationships between each author are not all related because each author has their own topic area. This is shown by the total link strength of each author, the majority of which is still below 10. The total link strength shows

(Herlina, 2022). The image is a visualization with Density Visualization mode showing the research discussed in this paper. It can be seen from the picture below that the application of nanomedicine is still less than Parkinson's.

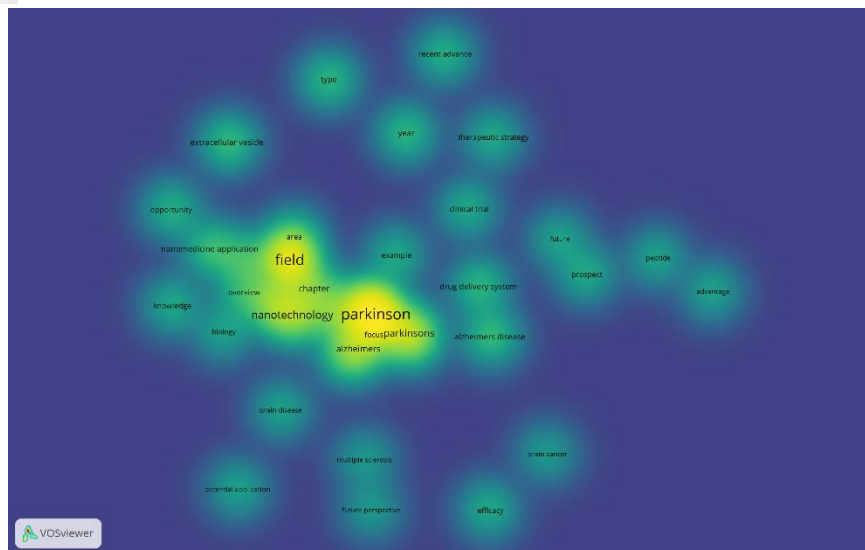


Figure 5 Density Visualization

Based on bibliometric analysis, it shows that the number of documents, highest citations, publisher distribution analysis and visualization using VOSviewer published about the application of nanomedicine for Parkinson's is still quite low. This shows that there are still many opportunities to conduct research regarding the application of nanomedicine to Parkinson's disease because according to the World Health Organization (WHO), in the last 25 years, the prevalence of Parkinson's disease has doubled.

Conclusion

Based on the findings that have been obtained regarding the application of nanomedicine to Parkinson's disease which are reviewed based on publication trends in the 2017-2022 range with an increase in publications each year, based on the most citations which have more than 100 citations consisting of 20 articles from various publisher sources. Meanwhile, in the co-occurrence analysis using VOSviewer, it was shown that in the network visualization the keywords that frequently appeared were "Parkinson", "field", and "Nanotechnology". In the overlay visualization the keywords "Parkinson's" and "nanomedicine" are not articles that discuss the most recent research. However, if you look at the topic density in "Nanomedicine" it is still small. So it is concluded that this research can help researchers determine the topics to be researched and can also be a reference for research related to the application of nanomedicine to Parkinson's disease.

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