

Applied of bioinformatics in drug discovery and drug development: bioinformatic analysis 1996-2024

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Abstract. Drug discovery and drug development were two complex process to find new drugs. Advance science of medicine after human genome project were established accelerating the development of new field called bionformatics. Currently, bioinformatics integrated multidisciplinary studies including molecular biology, mathematics and information engineering. This study utilized the Biblioshiny and VosViewer databases as well as the Scopus database to evaluate the study related to the bioinformatics in Drug Discovery and Drug Development. Our study were analyzed the scopus data which were retrieved from 1996-2024. We highlighted that 1581 research articles which were published in 701 journals. Our findings showed that the annual grow up of the research related study was increased annually with the peak of study in 2023. Besides, top five most relevant sources of study was PlosOne (32 documents), international journal of molecular sciences (30 documents), BMS Bioinformatics (29 documents), Bioinformatics (24 documents), and Frontiers in Genetics (19 documents). In conclusion, through the integration of the use of Vosviewer, biblioshiny and Scopus database software, our findings show a positive trend regarding research on the application of bioinformatics in drug discovery and drug development.

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1 Introduction

Drug discovery were initially begins with the diagnosis of a disease with characteristic symptoms that reduce the quality of life. Conventionally, drug discovery is a chemical (which can be a simple chemical or a complex protein) or a combination of chemicals that reduces symptoms without causing severe side effects in the patient. Other desirable properties of a drug include affordability and profitability for drug companies [1]. There is a low chance of drug resistance [2], [3] which causes a drastic reduction in term of cost drug, low environmental impact [4]. Therefore, the ideal of drug discovery is not only propose the efficacious with few side effects, but also has minimal long-term negative effects on patients, society and the environment. Drug development is a complex, lengthy, expensive due to the process requires it to be tested on humans. The last few decades showed that the exponential increase in the complexity and cost of clinical development without a commensurate increase in success rates [5]. Perhaps most impactful is the challenging of translation of advances in basic science, such as advances driven by genome discovery, into clinical applications. Challenging translation means that drugs that enter clinical development without sufficient supporting evidence are more likely to fail, and often do so after costly human testing [6].

Bioinformatics is an interdisciplinary science that includes genomics, transcriptomics, proteomics, population genetics, and molecular phylogenetics [7]. Bioinformaticians in drug discovery use high-throughput molecular data in comparisons between symptomatic carriers (patients, animal disease models, cancer cell lines, etc.) and normal controls [8]. The main goal of such comparisons is to relate disease symptoms to genetic mutations, epigenetic modifications, and other environmental factors that modulate gene expression. identify drug targets that can restore cellular function or eliminate non-functioning cells, such as cancer cells, predict or refine drug candidates that can act on drug targets to achieve designed therapeutic outcomes and minimize side effects, and assess environmental health impacts and potential resistance drug [9]. The development of modern bioinformatics cannot be separated from the development of biotechnology in the 70s, where an American scientist made innovations in developing recombinant DNA technology. Thanks to this discovery, the first biotechnology company in the world was born, namely Genentech in the US, which then produced the insulin hormone protein and bacteria needed by diabetes sufferers. So far, insulin can only be obtained in very limited quantities from the cow's pancreas [10].

Bioinformatics is the application of computational and analytical tools to interpret biological data [11]. At this time, bioinformatics has developed into a study that combines the disciplines of molecular biology, mathematics, and information engineering [12]. The study of bioinformatics cannot be separated from the development of modern molecular biology, which is characterized by the human ability to understand the genome, namely the blueprint of genetic information that determines the characteristics of each living creature which is encoded in the form of DNA (deoxyribonucleic acid) molecular bands [13]. The ability to understand and manipulate the DNA genetic code is greatly supported by information technology through hardware and software. One of the early contributions of bioinformatics to drug target discovery was the identification of PCSK9 inhibitors for lower low-density lipoprotein (LDL), or “bad,” cholesterol [14], [15]. Current developments in new drug discovery will become more effective when combined with many scientific disciplines including bioinformatics and OMICS data [16]. our study in line with one of the agenda of Sustainable Development Goals (SDG's) were to ensure healthy lives and promote well-being for all, at all ages. To achieve this goal, many things can be done, including mapping collaborative research between countries that can mutually strengthen each other. So the research we are conducting is part of the method to achieve the SDG's goals.

Bibliometric analysis is one of the most widely used methods for assessing the credibility, quality and impact of a scientific work worldwide [17]. One of the efforts for this analysis is

to relate the frequency of citations to the number of articles cited by researchers. Therefore, scientific papers will benefit from the most frequently cited articles [18]. In addition, bibliometrics serves as a tool for discovering understudied research topics within a particular disciplinary field. This generates new research ideas [19]. Bibliometric analysis related to applied of bioinformatics in drug discovery and drug development studies to find out whether the research is interesting to carry out [20]. Information about research on the application of bioinformatics in drug discovery and drug development is presented in bibliographic data. Because it can help turn publication metadata into more manageable maps or visualizations to obtain useful information, such as keywords to determine research themes in a particular discipline, author affiliation with a particular journal to determine the geographic scope of the journal, and institutional collaboration, bibliometric mapping is very helpful both the scientific community and the general public. The aim of this study is to provide an overview of research trends in the application of bioinformatics in drug discovery and drug development globally.

2 Material and Methods

2.1 Database

SciVerse Scopus is one of the databases that can be accessed online to find the documents related to the bioinformatics in drug discovery and drug development (accessed on 01/05/2024). The Scopus database was chosen because it has many prominent advantages compared to other online databases [21]. First, this database provides information with a number of features that make selection and categorization easier, such as country, author, journal, and institution. Second, this database also provides a number of citations for each group of documents, which serves as a matrix for determining the reputation of scientific research [22].

2.2 Bibliometric Indicator

The bibliometric analysis criteria used are as follows: (1) document type and language; (2) publication developments; (3) keywords that are more widely used by researchers; (4) analysis of citations and number of articles cited; (5) the ten most cited countries; (6) the top ten most active journals; and (7) international collaboration. Data on active and most cited publications is collected directly from top international journals. Besides, data on publications with the most citations comes from Scopus by counting articles and citations for each country every year. Two Software application programs were utilized to display bibliometric maps. including *VOSViewer version 1.6.16* [23] Biblioshiny [24].

2.3 Keywords and Search Strategy

We filtered the documents using a keyword search engine through Scopus Search <https://www.scopus.com/search/form.uri#basic>. Table 1 provides a description of specific search for Bioinformatics in Drug Discovery and Drug Development. All research-related publications were found through a publication search from 1996 to 2024 with the keywords “Bioinformatics”, “Drug Discovery”, and “Drug Development” To find the exact phrase in Scopus, the citation mark (“”) is used, while the asterisk (*) is used to find all possible related keywords (Wildcard). We create a strategy for the title, abstract, or keywords that combines all the terms and phrases that might be relevant.

3 Results and Discussion

The aim of current study to analyze the trend of application of bioinformatics in drug discovery and drug development during period 1996-2024. This research utilizes documents that have been published in the Scopus database from 1996-2024. The database retrieved from the Scopus database was analyzed using VOSViewer [25] and Biblioshiny R [26]. Our study provided the information related the application of boinformatics in drug discovery and drug development including most author keywords; Document Type and Language; Trend Publication; Source of documents; The Most relevant affiliation related to the Trend of Application of Bioinformatics in Drug Discovery and Drug Development during period 1996-2024; The most productive country in publications; Collaboration among authors in multiple continents; Citation Analysis and Number of Articles Cited.

3.1 Most Used Keywords

The database collected from the Scopus database was analyzed using *VOSViewer* and Biblioshiny R. We obtained the main information regarding studies related to the application of bioinformatics in drug discovery and drug development which presents information about study the data over a period of time from 1996 to 2024. The results of this analysis have inclusion criteria in the form of documents in English, so that all documents other than English will be excluded. During the period from 1996 to 2024, from the Scopus database, studies related to the application of bioinformatics in drug discovery and drug development were obtained in top 10 subject areas including Biochemistry, Genetics, and Molecular Biology (902), Medicine (570), Pharmacology, Toxicology and Pharmaceutics (356), computer science (256), immunology and microbiology (213), chemistry (182), mathematics (117), chemical engineering (98), agricultural and biological sciences (86), Neuroscience (81), Multidisciplinary (53). This relates to the availability of sources and types of references that can be used in research related to the application of bioinformatics in drug discovery and drug development. In mapping author keyword types using VOSviewer software, both the thickness of the connecting line and the distance between two keywords reflect the extent of the relationship between the words. When using VOSviewer to map the author's most frequent keywords, node size keywords represent the frequency of occurrence that keyword. Color indicates the newness of the information, where yellow indicates the newness of the keywords used by researchers; while the blue line shows that the research area has been used in the field of science for over longer time.



The most often keywords used by authors include system biology, genomics, biomarkers, machine learning, and target identification cancer. Bioinformatics keywords also appear as keywords used by the author. Figure 1 shows the breadth of keywords used and their relationship to other keywords. The bibliometric mapping results from the VOSViewer application show that the more frequently there are pairs of two keywords, the closer the relationship between the keywords (Figure 1). Keywords that are interrelated are bioinformatics, biomarker with target identification, and genomics [16].

Based on main information related to bioinformatics for drug discovery and development, Table 1 presents quantitative data covering the time span of the research period taken from 1996 to 2024. Sources include journals, books, and others used as references, then the total of documents used analyzed were 7011 documents and obtained an Annual Growth Rate of 13.6% Percentage of annual growth of documents. The average number of citations per document was 26.92. The average number of citations received per document from all documents resulted in the number of references used in the research being 83,727 documents. It can be concluded from 7011 documents that the number of authors who contributed was 7807 people with 87 single authors who produced 91 documents. With an average growth of authors per document of 6.39. Meanwhile, International Collaboration has a percentage value of 23.78%. Documents such as articles show that the authors published the most with a total of 1581 documents. This certainly provides important insights into bioinformatics research statistics over time, such as growth rates, citation metrics, and authorship patterns that show how research in this field is carried out is important in the Applied of Bioinformatics in Drug Discovery and Drug Development.

Table 1. Main Information related Bioinformatics for Drug Discovery and Drug Development

Description	Results
MAIN INFORMATION ABOUT DATA	
Timespan	1996:2024
Sources (Journals, Books, etc)	701
Documents	1581
Annual Growth Rate %	13.6
Document Average Age	6.27
Average citations per doc	25.92
References	83727
DOCUMENT CONTENTS	
Keywords Plus (ID)	17817
Author's Keywords (DE)	4305
AUTHORS	
Authors	7807
Authors of single-authored docs	87
AUTHORS COLLABORATION	
Single-authored docs	91
Co-Authors per Doc	6.39
International co-authorships %	23.78
DOCUMENT TYPES	
Articles	1581

3.3 Trend Publication

The trend of publication is important to noted related the drug discovery and drug development, therefore our study provide the specific information during 1996-2024. The graph of annual scientific production trends related to Bioinformatics for Drug Discovery and Development shows an increase in the number of articles annually Figure 2. The following are the main points of significant increase. Starting with a relatively low number in 1997, there was a significant increase around 2023. The peak production of the number of articles reached its peak around 2017. A slight decrease after reaching the peak, there was a light decrease in 2018. Overall Trend in general overall, the graph shows an upward trend in research and publications in this field over two decades, indicating growing interest and progress in bioinformatics applied to drug discovery and development.

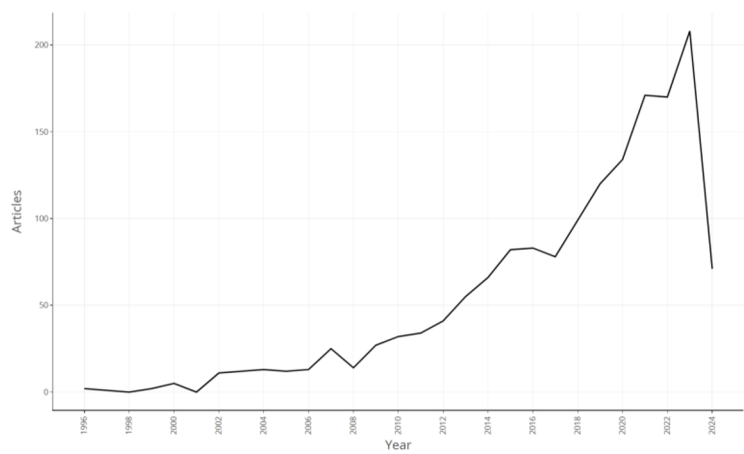


Fig. 2. Annual Scientific Production Trend related to Bioinformatics for Drug Discovery and Drug Development

3.4 Source of documents

In Figure 3, there are 10 journals which show the number of documents published by various scientific journals in certain fields. The following are several important points based on publication trends. The most productive journal was Plos One with a total number of documents were 32; followed by the International Journal of Molecular Sciences (30 documents). The third most productive journal was BMC Bioinformatics with 29 documents. Frontiers in Genetics (19 documents), frontiers in Immunology (18 documents), Nucleic Acids Research (18 documents), journal of Chemical Information and modeling (16 documents), briefings in Bioinformatics (14 documents), and oncology letters (14 documents) It shows the most relevant sources regarding trends in Bioinformatics for Drug Discovery and Development based on This figure is important for visually representing the volume of research activity in the field of bioinformatics in various scientific publications.

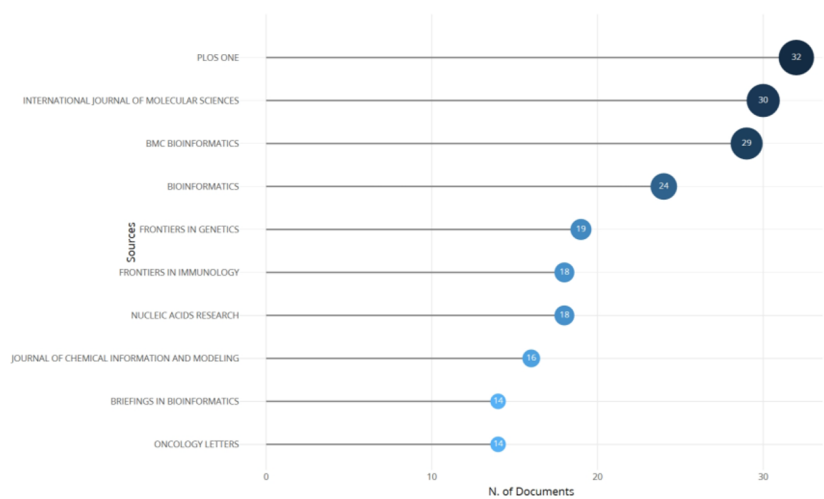


Fig. 3. Most relevant sources related to the Trend of Bioinformatics for Drug Discovery and Drug Development

3.5 The Most relevant affiliation

In (Supplementary Figure 1) Shows the 10 most relevant affiliations regarding Bioinformatics trends for Drug Discovery and Development. From the top 10, Central South University: Has the highest number of articles, around 77 documents, while Huazhong Medical School has a fairly high number of published articles, namely 38 documents, then University of California is included in the list of affiliates with significant publications and Other Institutions: Including Zhejiang University, Peking University Health Science Center, and others who actively publish in this area. This study highlights an important information because it shows which institutions are most active in publishing in the field of bioinformatics for drug discovery and development.

3.6 The Most productive country in publications

Based on the visualization in (Supplementary Figure 2) there are the most productive countries in publishing research related to Bioinformatics for Drug Discovery and Development. The country of China stands out as a center with large nodes and many connections, indicating a high volume of publications. The United States and the United Kingdom also have large nodes and many connections, indicating significant contributions in this field. International Cooperation in (Supplementary Figure 2) shows collaboration between countries, which is marked by lines connecting the names of countries. Time Period The data covers publications from 1996 to 2024, providing an overview of research trends over that period. The figure provides an overview of how countries collaborate and contribute to research in bioinformatics focused on drug discovery and development. China appears to be leading in terms of number of publications, with the United States and the United Kingdom also playing an important role in the advancement of this field. International collaboration shows the importance of global cooperation in scientific research.

3.7 Collaboration among authors from multiple continents

Research collaboration and networking to increase national preparedness and management of drug discovery and drug development. Based on our findings in (Supplementary Figure 3), China is the country with the largest number of collaborating countries, followed by the United States and India which are ranked second and third respectively. Visualization of productive cooperation collaboration between countries with a minimum of 50 documents. Contributions and collaborations of authors from developed countries such as China and the United States still dominate this research, followed by India, England and Germany. Authors from Indonesia still contribute little to research related to Bioinformatics for Drug Discovery and Drug Development. This could be an opportunity for educational institutions in Indonesia to increase the production of scientific work with the aim of sharing knowledge, ideas and technology in order to compete with other countries in Southeast Asia. Even though Indonesia is a developing country, it can collaborate with other countries to increase the production of scientific work to contribute to the development of science, especially drug development.

3.8 Citation Analysis and Number of Articles Cited

We found the Top 10 cited articles related to the Bioinformatics for Drug Discovery and Drug Development during period 1996 to 2024 (Table 2). In the journal Nucleic Acids Res by the author Daina regarding the Bioinformatics for Drug Discovery and Drug Development entitled "SwissTargetPrediction updated data and new features for efficient prediction of

protein targets of small molecules” was cited the most 1681 times with an average of 280.17 citations per year [27]. Followed by Okada y et al which were published in the journal Nature [28] « Genetics of rheumatoid arthritis contributes to biology and drug discovery. Considering the information above, we believe that this journal will evolve into a widely cited article regarding Bioinformatics research for Drug Discovery and Drug Development in the future. Additionally, this information will provide researchers with journal sources that can assist them in choosing the best journal for their research [29].

Table 2. Top 10 cited articles related to the Bioinformatics for Drug Discovery and Drug Development

Paper	Year	Journals	PMID	Total Citations	TC per Year	Normalized TC
Daina A	2019	Nucleic Acids Res	31106366	1681	280.17	42.57
Okada Y	2014	Nature	24390342	1629	148.09	27.88
Northcott Pa	2011	J Clin Oncol	20823417	1045	74.64	11.86
Chandrashekar Ds	2022	Neoplasia	35078134	647	215.67	58.07
Liu Z	2016	Sci Rep	26879404	625	69.44	17.96
Pan Z	2007	Chemmedchem	17154430	571	31.72	7.35
Daina A	2014	J Chem Inf Model	25382374	565	51.36	9.67
Shergalis A	2018	Pharmacol Rev	29669750	505	72.14	15.34
Chen X	2013	Bioinformatics	24002109	500	41.67	11,13
Dudley Jt	2011	Bioinform Brief	21690101	417	29.79	4.73

PMID: PubMed unique identifier

Bioinformatics uses computational tools to analyze biological data, which contributes to drug discovery and development [9]. This analysis aids in identifying drug targets, streamlining the drug development process, and forecasting the efficacy of potential medications. Bioinformatics accelerates the drug discovery process by providing insight into the interactions between drugs and biological systems, eventually leading to the development of more effective and targeted drugs [30]. Bioinformatics is also used for translational drug discovery in infectious diseases. For example, the presence of a viral or bacterial infection results in a specific gene expression profile in the cell. Comparing these profiles to other disease profiles and drug-induced genetic profiles provides opportunities for repositioning against existing drugs [31].

The bibliometric analysis conducted in this study identified China, the United States, and the United Kingdom as the most productive countries in bioinformatics research for drug discovery. This is the first study to analyze drug discovery and development bibliometrics from 1996 to 2024. The majority of articles about drug discovery are written in developed countries, while developing countries continue to show an insignificant trend. So this is certainly a criticism for the future, especially since research related to herbal medicine is conducted in developing countries. There are limitations to this study due to the methodological approach used for the bibliometric analysis. It is possible for bibliometric studies based on Scopus data to produce false positives and false negatives. As a result of the emphasis of English-language journals, Chinese, Japanese, and other languages are undervalued. As multiple databases cannot be combined and analyzed for bibliometric analysis, only one database is required.

4 Conclusion

This study demonstrates how bioinformatics plays an important role in drug discovery and development by analyzing biological data with computational tools. Scopus data shows that publications have increased since 1996, with China, the United States, and the United Kingdom being the most productive countries in this research. International collaboration is also taking place, with China leading in terms of publications. Although Indonesian authors contributed little to this research, there is potential for future contributions. development. The most cited articles in this study were by Daina in 2019 and Chandrashekar in 2022, both of which discussed bioinformatics for drug discovery and development. Bioinformatics has helped identify drug targets and improve the drug development process, while bibliometric analysis aids in tracking bioinformatics-related research trends in drug discovery and development.

The Acknowledgements

This project was supported by grant from Bidang Publikasi Ilmiah (BPI) Universitas Ahmad Dahlan, Yogyakarta Indonesia. Authors also would like to thank Mr. Dr Zalik Nuryana for introducing us to the software of Biblioshiny and VosViewer.

Fundings

None

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors disclose no conflict.

Author contribution statement

L.M.Irham and W. Adikusuma conceived and designed the study. L. M.Irham and W. Adikusuma performed the computational analysis. L.M. Irham, D.P.Amukti wrote the manuscript. L.M.Irham provided the funding. D.P.Amukti, D.Singh and R Chong, M, Basyuni., S.Pranata., S.Khairi, I hilmi revised the manuscript. All authors have read and approved the manuscript and have made significant contributions to this study.

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