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Bibliometric Mapping Analysis of Research on Poly (Lactic-Co-Glycolic Acid) Nanoparticle in Drug Delivery Using VOSviewer

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Abstract

Poly/lactic-co-glycolic acid (PLGA) nanoparticles are one of the most effective biodegradable polymers in drug delivery systems in the human body. This research aims to study PLGA nanoparticles in drug delivery bibliometrically, mapping analysis using VOSviewer. Article data from the Google Scholar database using Publish or Perish. The keywords to search and collect relevant articles are "poly (lactic-co-glycolic acid)", "nanoparticle", "PLGA nanoparticle" and "drug delivery" (in the publication range 2013 to 2022). From the search results found 1000 articles relevant to PLGA nanoparticles in drug delivery. In the 2013-2022 period, the development of PLGA nanoparticle research was lacking, the peak of popularity occurred in 2019 with as many as 126 articles, and in the last 3 years, it has decreased. Further research on PLGA nanoparticles for drug delivery is associated with other terms such as immune response, antibody, targeted delivery, and controlled release.

Keywords: *Bibliometric, drug delivery, mapping analysis, PLGA nanoparticle, VOSviewer.*

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INTRODUCTION

Nanoparticles are solid colloidal protein particles measuring 10-400 nm [1] which are composed of natural or synthetic polymers [2]. The polymer can dissolve,

ensnare, encapsulate, adsorb or attach active substances such as drugs [1]. Various kinds of drugs, vaccines, and biological macromolecules can be delivered using nanoparticles [2]. Encapsulation of these molecules in nanocarriers can increase the solubility and stability of drugs as well as the therapeutic potential of drugs [1]. Nanoparticles as drug delivery are targeted to certain organs or cells [2].

Polymer nanoparticles are the most effective nanocarriers for targeted drug delivery. One of the polymers commonly used in the formation of nanoparticles is poly (lactic-co-glycolic acid) (PLGA), which is a biodegradable polymer that can be degraded into individual oligomers and monomers, where these individual oligomers and monomers undergo metabolism in the body and can be excreted from the body through the normal path [1]. PLGA hydrolysis process in the body produces biodegradable monomer metabolites, that is lactic acid and glycolic acid [3]. Both monomers are only metabolized in the body via the Krebs cycle and are eliminated as carbon dioxide and air [1,4,5].

PLGA nanoparticles as biodegradable polymer nanoparticles are effective in drug delivery systems because of their ability to minimize systemic toxicity [6]. PLGA nanoparticles can reduce the side effects of drugs, reduce damage to cells, and reduce the recovery period [1,7]. Currently, PLGA-based nanoparticles are being investigated in cancer imaging and cancer therapy [2]. Thus, trend analysis in this research is very helpful in the further development of PLGA nanoparticles in drug delivery.

The development of research on PLGA nanoparticles in drug delivery is known by bibliometric analysis techniques. The bibliometric method evaluates trends qualitatively and quantitatively [8]. Bibliometric analysis is a form of meta-analysis of bibliographic data from articles published in journals. This bibliometric analysis maps the trend of research visually so as to assist researchers in studying the development of the research. The software used is VOSviewer [9].

Studies on the bibliometric method were carried out on the neurotoxicity of nanoparticles [10], for the toxicity of algae nanoparticles [11], application of magnetite nanoparticles as drug delivery agents [12,13], production of nanocrystalline cellulose as drug delivery [14], biomedical applications of chitosan [15], chitosan with PVC polymer in biomedical applications [16], and biodegradable polymers for the development of environmental tracers [17].

Research on bibliometric analysis of PLGA nanoparticles in drug delivery using the VOSviewer application has not been carried out. Therefore, this study was conducted to examine the development of research on PLGA nanoparticle in drug delivery and indexed by Google Scholar. This research is important because PLGA nanoparticles are effective in drug delivery systems and have the potential to be applied in cancer imaging and cancer therapy. The bibliometric approach with mapping analysis using VOSviewer helps in creating new research related to PLGA nanoparticles for drug delivery. The results of this study are expected to increase further research on PLGA nanoparticles in drug delivery and be associated with other terms such as immune response, antibody, targeted delivery, and controlled release.

METHODS AND ANALYSIS

Bibliometric Mapping Analysis of Research on PLGA Nanoparticles in Drug Delivery Using Vosviewer refers to research [18]. This study uses research article data

from Google Scholar-indexed journals. Google Scholar was chosen because its database is open source. The stages of the research carried out are: (i) collection of publication data using the Publish or Perish application; (ii) processing of bibliometric data for articles that have been obtained using the Microsoft Excel application; (iii) computational mapping analysis of bibliometric published data using the VOSviewer application; (iv) analysis of computational mapping analysis results.

The keywords used in collecting publication data using Publish or Perish are "poly (lactic-co-glycolic acid)", "nanoparticle", "nanoparticle PLGA", and "drug delivery" with a time span of 2013-2022. The articles that have been collected are saved in *.ris and *.csv formats. Data *.ris format was analyzed using VOSviewer to visualize and evaluate trends in bibliometric maps. While data in *.csv format were processed using Microsoft Excel. VOSviewer has 3 mapping variations, that is network visualization, density visualization, and overlay visualization. At the bibliometric mapping stage, keywords that are less relevant are not used.

RESULTS AND DISCUSSIONS

Result of publication data search

Based on the results of the Google Scholar database search using the Publish or Perish software, 1000 articles were obtained according to the research criteria. Table 1 shows 10 examples of relevant article data for PLGA nanoparticles in drug delivery from the Publish or Perish search. The Publish or Perish search results provide information on the number of citations as much as 37559, per year as many as 4173.22, per article 37.56, average h-index of 82, and g-index of 147.

Research developments related to PLGA nanoparticles in drug delivery

Figure 1 shows the development of research on PLGA nanoparticles in drug delivery in Google Scholar-indexed journals in the last 10 years. Based on the figure 1, it can be seen that during 2013-2022, the publication of research results on PLGA nanoparticles in drug delivery fluctuated. High popularity occurred in 2018-2019 and the peak of popularity occurred in 2019 with the publication of 126 articles. In the range of 2020-2022, research on PLGA nanoparticles in drug delivery decreased. The fluxtua-

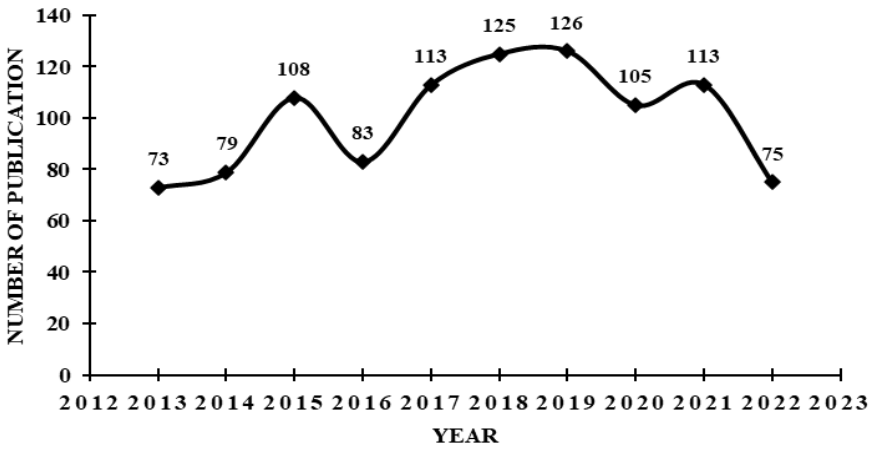

Figure 1 Development level of PLGA nanoparticle research in drug delivery

Table 1 Publication data of PLGA nanoparticles in drug delivery

No	Author	Title	Year	Cites
1	Manoochehri et al.	Surface modification of PLGA nanoparticles via human serum albumin conjugation for controlled delivery of docetaxel	2013	114
2	Mirakabad et al.	PLGA-based nanoparticles as cancer drug delivery systems	2014	332
3	Fornaguera et al.	PLGA nanoparticles prepared by nano-emulsion templating using low-energy methods as efficient nanocarriers for drug delivery across the blood–brain barrier	2015	172
4	Bi et al.	Intranasal delivery of rotigotine to the brain with lactoferrin-modified PEG-PLGA nanoparticles for Parkinson's disease treatment	2016	129
5	Mosafer et al.	In vitro and in vivo evaluation of anti-nucleolin-targeted magnetic PLGA nanoparticles loaded with doxorubicin as a theranostic agent for enhanced targeted cancer imaging and therapy	2017	104
6	Sánchez-López et al.	Memantine loaded PLGA PEGylated nanoparticles for Alzheimer's disease: In vitro and in vivo characterization	2018	128
7	Cappellano et al.	Exploiting PLGA-based biocompatible nanoparticles for next-generation tolerogenic vaccines against autoimmune disease	2019	58
8	Arafa et al.	Chitosan-coated PLGA nanoparticles for enhanced ocular anti-inflammatory efficacy of atorvastatin calcium	2020	36
9	Operti et al.	PLGA-based nanomedicines manufacturing: Technologies overview and challenges in industrial scale-up	2021	33
10	Hashemi et al.	Mitoxantrone-loaded PLGA nanoparticles for increased sensitivity of glioblastoma cancer cell to TRAIL-induced apoptosis	2022	4

ting popularity is due to the interest and limitations of the research needs of PLGA nanoparticles in drug delivery. The lack of up-to-dateness is one of the factors that cause a decrease in interest in this research.

Topic visualization of PLGA nanoparticles in drug delivery using VOSviewer

Computational mapping article data using VOSviewer. From the results of the mapping, 228 items were found. Each item found in the mapping of data related to PLGA nanoparticles in drug delivery is divided into 8 clusters, that is:

(i) Cluster 1 marked in red has 42 items of which acetonitrile, acid nanoparticle, aptamer, assessment, biocompatibility, cancer cell, cell-penetrating peptide,

characterization, comparative study, conjugation, delivery system, development, dl lactic co glycolic acid, docetaxel, doxorubicin, formic acid, growth factor, investigation, kDa, lactic, lactide co glycolic acid, loaded poly, lung cancer, micro, microRNA, nano, nanocarrier, nanoparticle preparation, peg, phosphoric acid, plga nps, plga peg, polyvinyl alcohol, polyethylene glycol, potential, targeted delivery, trifluoroacetic acid, tumor, type, vitro, vivo evaluation, and vivo study.

(ii) Cluster 2 is marked in green and has 36 items of which activity, antitumor efficacy, application, approach, bioavailability, biodegradable material, biodegradable polymer, controlled delivery, curcumin, degradation, efficiency, enhancement, formulation, hyaluronic acid, immune response, l lactide co glycolide, nanoparticle formulation, nanoparticle suspension, nanoparticle system, nps, particle size, pdi, plga, nanopartikel PLGA, poly dispersity index, poly l lysine, poly lactic co glycolic acid, poly lactic co glycolic acid nanoparticle, polymer, protective effect, quercetin, resveratrol, size, stability, surfactant, and synthetic polymer.

(iii) Cluster 3 is marked in dark blue and has 31 items of which advantage, analysis, biodegradable nanoparticle, block poly, challenge, controlled release, copolymer, drug release, ethylene glycol, glycol, glycolide, human serum albumin, hydrogel, impact, influence, insulin, interaction, lactic co glycolic acid, lactide, lactide co, lactide co glycolide, methoxy poly, micelle, nanoparticle size, nanoparticle surface, oral delivery, peg plga, polyester, role, transmission, and use.

(iv) Cluster 4 is marked in yellow and has 29 items of them acetic acid, antibody, based nanoparticle, brain delivery, breast cancer, chemotherapy, co-delivery, co glycolic acid, delivery, drug delivery, efficacy, fluorouracil, glioblastoma, inhibition, lactic co glycolic acid, ligand, liposome, magnetic nanoparticle, methotrexate, nanoparticle, nanotechnology, phosphotungstic acid, plga np, siRNA, sorafenib, strategy, system, treatment, and uptake.

(v) Cluster 5 is marked with purple color and has 26 items of them anticancer activity, bone regeneration, characteristic, co polymer, comparison, dl lactic co glycolic, effect, encapsulation, fda, folic acid, hydrochloric acid, lactic acid glycolic acid, microsphere, particle, plga microsphere, poly, production, pva, ratio, spray, surface, surface modification, time, vinyl alcohol, vitro evaluation, and vivo.

(vi) Cluster 6 is marked in light blue and has 25 items of which ability, agent, anti-inflammatory, average mw, biodegradable poly, blood brain barrier, carrier, disease, dl lactide, dl lactide co glycolide, drug, drug delivery system, evaluation, fabrication, fatty acid, gemcitabine, glycolic acid, l lactic co glycolic acid, lactic acid, lipid, microparticle, oleic acid, property, vitro study, and zeta potential.

(vii) Cluster 7 is marked in orange and has 20 items in between caprolactone, characterization, chitosan, cytotoxicity, dexamethasone, gelatin, lactic co glycolic, nanofiber, nanoparticle uptake, nanoprecipitation, pcl, pla, plga poly, poly lactic acid, polycaprolactone, polylactic acid, polymeric nanoparticle, preparation, synthesis, and transport.

(viii) Cluster 8 is marked in brown and has 19 items in between acid, ascorbic acid, bloodbrain barrier, cancer, cancer therapy, drug delivery application, hydrolysis, matrix, molecular weight, nanoparticle characterization, nucleic acid, optimization, peptide, pga, PLGA nanoparticles, polyglycolic acid, protein, therapy, tpgs.

The relationship between one term and another is shown in each existing cluster. Each term is labeled with a colored circle. Each term has a different circle size depending

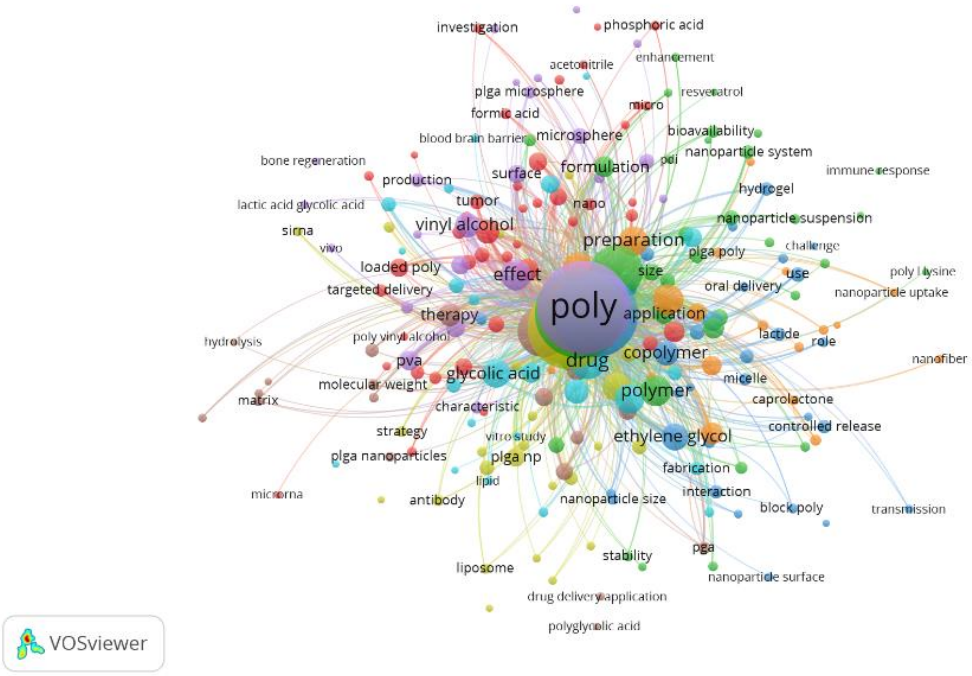

Figure 2 Network visualization on keywords PLGA nanoparticles in drug delivery

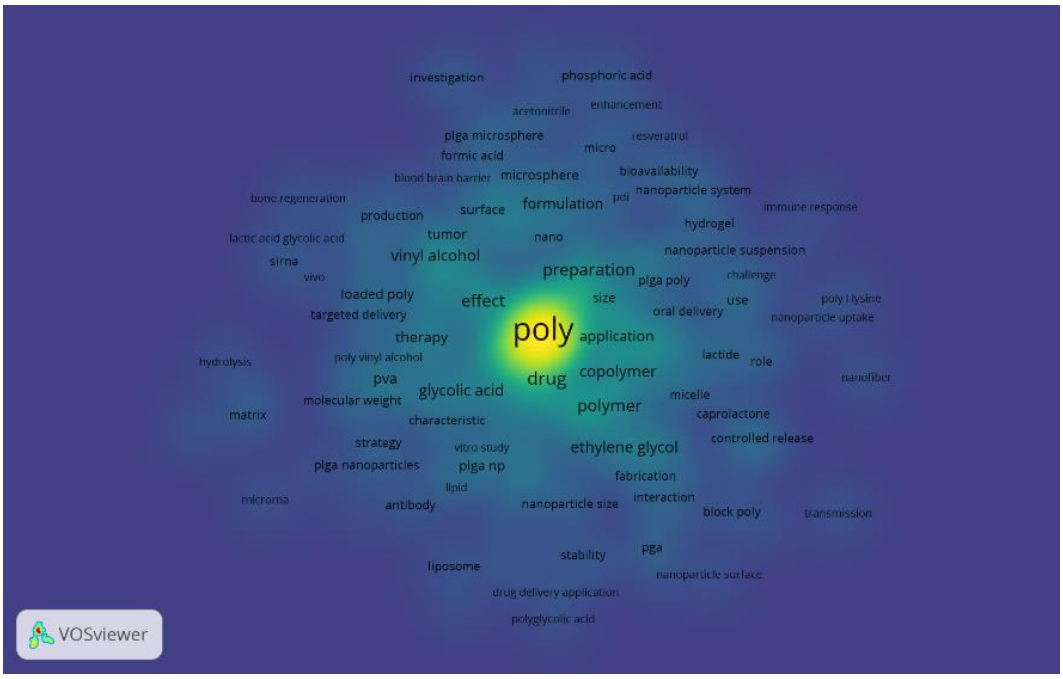

Figure 3 Density visualization on keywords PLGA nanoparticles in drug delivery

on the frequency of occurrence of the term in the title and abstract [19]. The more the term is found in the title and abstract of an article, the larger the circle size [8]. The mapping visualization analyzed in this study consists of 3 parts, namely network visualization (see Figure 2), density visualization (see Figure 3), and overlay visualization (see Figure 4).

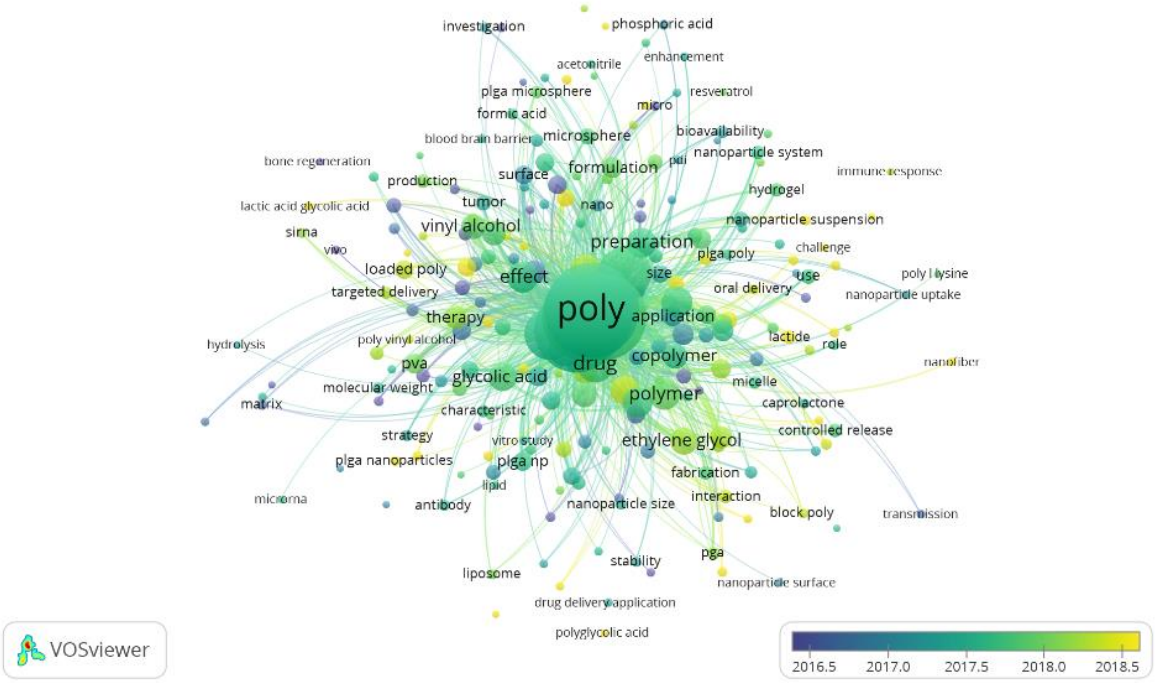

Figure 4 Overlay visualization on keywords PLGA nanoparticles in drug delivery

Figure 2 shows the relationship between terms in a cluster of related and researched research topics of PLGA nanoparticles in drug delivery. The relationship between these terms is described in an interconnected network. Based on the clusters contained in the network visualization, it can be seen that the research on PLGA nanoparticles in drug delivery is divided into 4 fields, namely the term PLGA which belongs to cluster 2 with a total of 227 links, 5539 total link strength, and 748 occurrences (see Figure 5). The second term is nanoparticles belonging to cluster 4 with a total of 227 links, 4617 total link strengths, and 641 occurrences (see Figure 6). The third term is PLGA nanoparticles belonging to cluster 2 with a total of 212 links, 2024 total link strengths, and 262 occurrences (see Figure 7). The last term is drug delivery which belongs to cluster 4 with a total of 173 links, 794 total link strengths, and 111 occurrences (see Figure 8).

Figure 3 shows density visualization which means the brighter the yellow color and the larger the circle diameter of a term, the more often the term appears [19]. This means that a lot of research has been done on the term. On the other hand, if the color of the term fades closes to the background color, then the number of studies related to the term is small. Based on Figure 3, it can be seen that in general, research related to PLGA nanoparticles in drug delivery has a small number of studies.

Figure 4 is an overlay visualization showing the novelty of research on related terms in the study of PLGA nanoparticles in drug delivery [19]. Figure 4 which is clarified in Figure 9 shows that research on PLGA nanoparticles in drug delivery was carried out from mid-2017 to 2018. The popularity of research on PLGA nanoparticles in drug delivery is quite old so through the results of this study we can easily make new research on the topic.

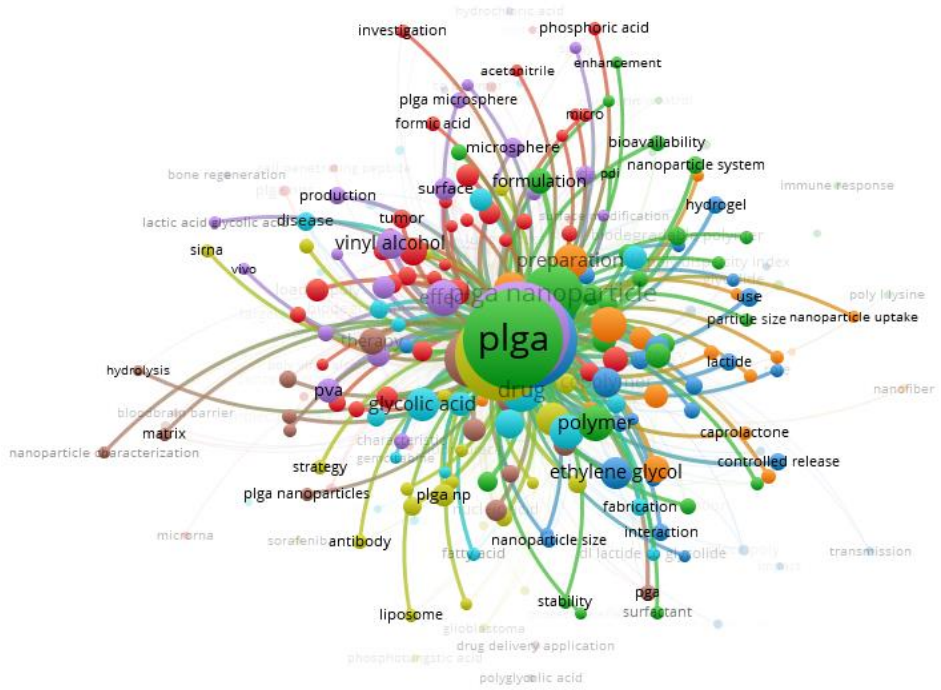

Figure 5 Network visualization for the term PLGA

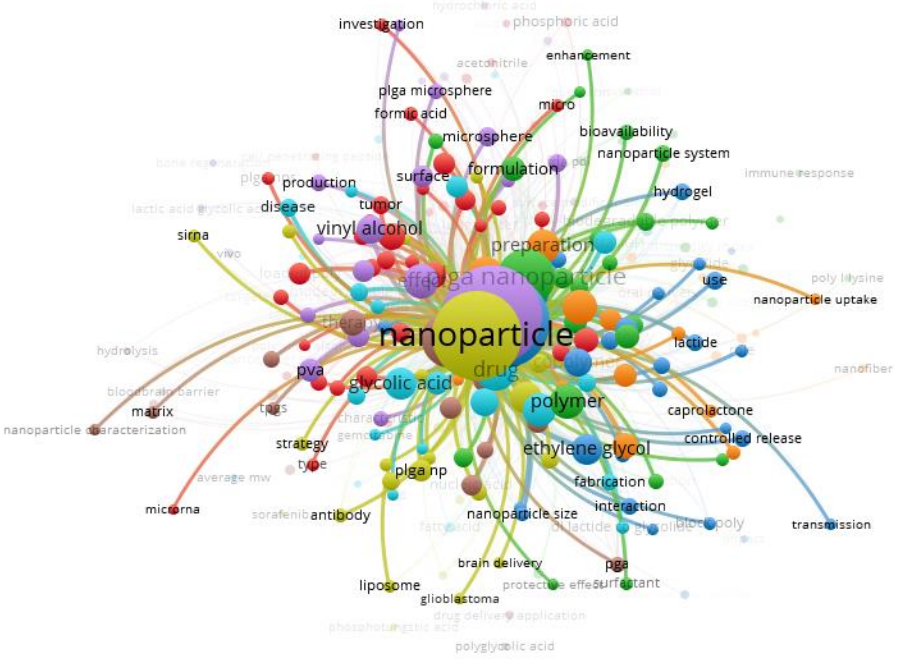

Figure 6 Network visualization for the term nanoparticle

Figure 5 shows the relationship network between the term PLGA and other terms, namely glycolic acid, polymer, ethylene glycol, investigation, phosphoric acid, enhancement, acetonitrile, PLGA microsphere, formic acid, micro, microsphere, bioavailability, formulation, surface, pdi, nanoparticle system, hydrogel, tumor, vinyl alcohol, production, disease, vivo, vanish, hydrolysis, matrix, pva, strategy, nanoparticle PLGA, antibody, liposome, plga np, nanoparticle size, stability, pga, interaction, fabrication, controlled release, caprolactone, lactide, particle size, nanoparticle uptake, use.

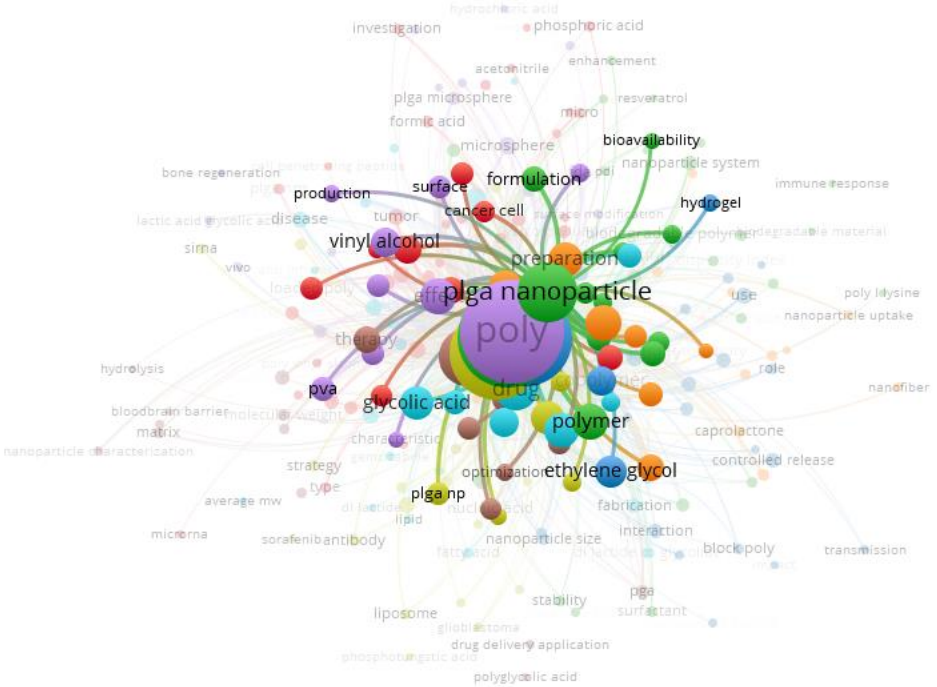

Figure 7 Network visualization for the term PLGA nanoparticle

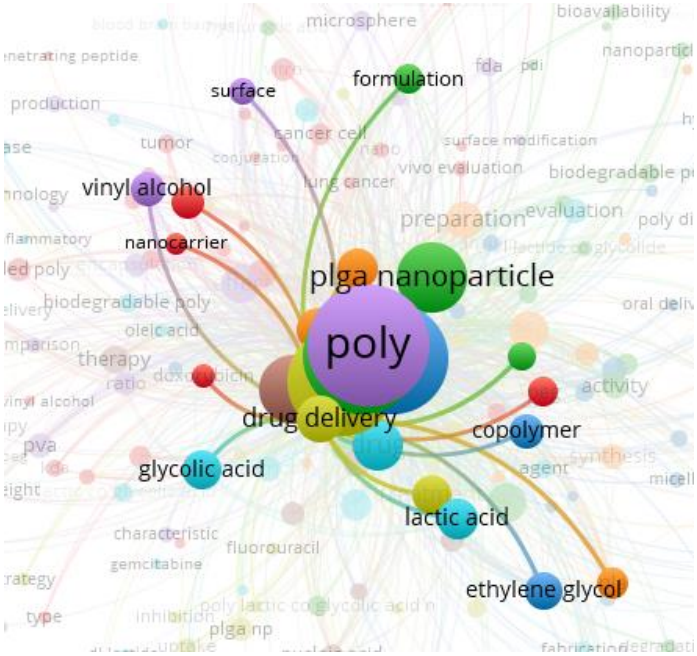

Figure 8 Network visualization for the term drug delivery

Figure 6 shows the relationship network between the term nanoparticle and other terms, including glycolic acid, polymer, ethylene glycol, investigation, enhancement, PLGA microsphere, formic acid, micro, microsphere, bioavailability, formulation, surface, nanoparticle system, hydrogel, tumor, vinyl alcohol, production, disease, siRNA, matrix, pva, strategy, antibody, liposome, plga np, nanoparticle size, pga, interaction, fabrication, controlled release, caprolactone, lactide, nanoparticle uptake, use, microrna, type, glioblastoma, brain delivery, and transmissions. Figure 7 shows the relationship network between PLGA nanoparticles with other terms, namely bioavaibi-

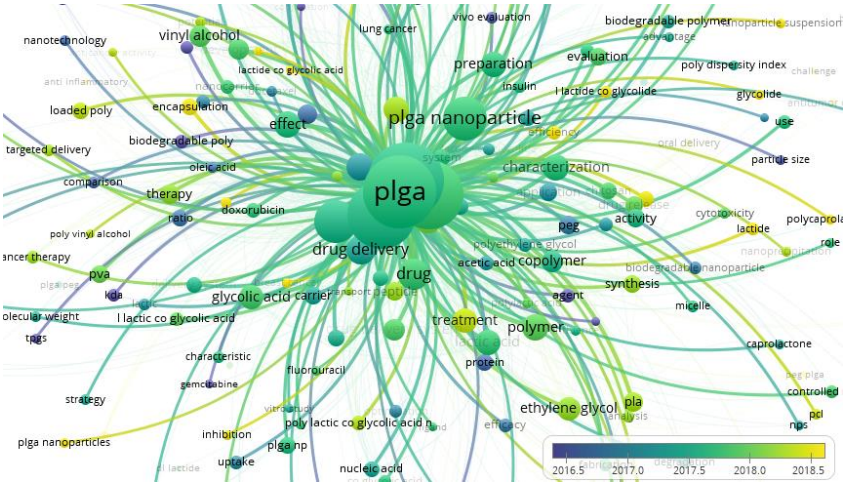

Figure 9 Overlay visualization of PLGA nanoparticles in drug delivery in mid-2017 to 2018

lity, formulation, hydrogel, surface, cancer cell, production, surface, vinyl alcohol, pva, glycolic acid, plga np, ethylene glycol, and polymer. Figure 8 shows the network of relationships between the term drug delivery with other terms, including poly, nanoparticle PLGA, glycolic acid, lactic acid, ethylene glycol, copolymer, nanocarrier, vinyl alcohol, surface, and formulation.

Based on the data reported above, it is known that there is little relationship between the terms PLGA nanoparticles and drug delivery with other terms. The mapping results show that PLGA nanoparticles only have 212 links and are connected by 13 terms. Meanwhile, drug delivery only has 173 links and is linked to 11 terms. When compared with the terms PLGA and nanoparticles which are associated with various terms, each associated with 42 terms and 38 terms, it can be concluded that PLGA nanoparticles in drug delivery are still very likely to be investigated further and associated with other terms as a novelty of research. Through the research of this bibliometric mapping analyst, we can look for more advanced research on PLGA nanoparticles in drug delivery.

CONCLUSIONS

Based on the results of the study, it is known that in the period 2013-2022 there were 1000 articles relevant to PLGA nanoparticles as drug delivery. During this period, the study of drug delivery PLGA nanoparticles was unstable. The popularity of research peaked in popularity in 2019 with 126 articles and has decreased over the last 3 years. Thus, this bibliometric mapping helps further research on PLGA nanoparticles in drug delivery and be associated with other terms such as immune response, antibody, targeted delivery, and controlled release.

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DECLARATION OF CONFLICTING INTERESTS

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