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Original Research

Liposomes, The Attractive Vehicles for Drug Delivery: A Scientometric Mapping of Web of Science Indexed Literature

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Abstract

The Liposome is a spherical-shaped vesicle composed of one or more phospholipid bilayers, closely resembling cell membranes' structure. It has a novel drug delivery system (NDDS); the lipid bilayer can fuse with other bilayers, such as the cell membrane, thus delivering the liposome contents. The present study has been conducted to map the research productivity of 'liposomes as drug delivery' between 1980 and 2021. This study employed the scientometric method to analyze 629 research papers indexed in the Web of Science database. Different bibliometrics indicators were used to assess the annual research growth, prolific authors, authorship pattern, funding agencies, productive source, organization, country, author keywords, cited paper and cited references, etc. Biblioshiny, Bibexcel, VOSviewer, and MS Office were used to analyze the 629 published papers. The findings show that 629 publications were published between 1980 and 2001, with 24674 citations. 2018 and 2019 recorded the highest research with 49 publications and 758 and 471 citations, respectively. Journal of Controlled Release was the most relevant source in the field, with 45 publications and 3063 citations. LIU Y was the most productive author, with 15 publications and 342 citations. Northwestern University USA has the highest record with 11 publications, and the USA was the most productive country with 181 publications, while China emerged as a leading collaborator with the USA (19 publications). Liposomes and cationic liposomes were identified as the most important research themes. Permeability, ocular drug delivery, Chemotherapy, Cancer therapy, Hypoxia, Combination therapy, and hyaluronic acid were research topics that have gained recent popularity. At the same time, Vesicles targeted drug delivery, cellular uptake, ultrasound, Chitosan, and Pegylation were identified as the research areas that require further attention in the field of liposomes as drug delivery research.

Keywords: Liposomes, Science Mapping, Scientometric, Research Assessment.

Introduction

Liposomes are microscopic vesicular structures consisting of bilayers formed spontaneously when phospholipids are dispersed in water. Liposomes are a novel drug delivery system that aims to deliver drugs at a directed rate and the place of action. Liposomes differ in size, composition, and charge. Liposomes are drug carriers loaded with drug molecules, proteins, nucleotides, plasmids, etc. Few drugs are formulated as liposomes to improve their therapeutic efficacy. Liposomes can be classified based on various criteria. Based on the size and number of bilayers, they are classified as multilamellar vesicles (MLV), large unilamellar vesicles (LUV), and small unilamellar vesicles (SUV). Based on composition, they are classified as conventional liposomes (CL), pH-sensitive liposomes, cationic liposomes, long-circulating liposomes (LCL), and immuno-liposomes. On the grounds of the method of preparation, they are classified as reverse-phase evaporation vesicles (REV), French press vesicles (FPV), and ether injection vesicles (EIV) (Yadav, Sandeep, Pandey & Dutta, 2017). Several advantages to applying a liposome as a drug delivery vehicle include improvement and control over pharmacokinetics and pharmacodynamics, target selection, decreased toxicity, and enhanced drug activity against intracellular and extracellular pathogens. However, there are a few disadvantages, such as short shelf life, stability, encapsulation efficacy, and sterilization complications.

Liposomes are the most studied drug delivery systems. A liposome is the first Nano-drug to receive FDA approval for clinical trials (Bobo, Robinson, Islam, Thurecht and Corrie (2016). Recent studies on the progress of nanomedicines reported that 56% of the research is on investigational liposomes (Ventola, 2017). Much research on liposomes has been done and published worldwide, and rigorous research has been carried out to develop liposomes as clinically significant drug-carrying vehicles. Liposomes were discovered by Alec D Bangham and R. W. Horne in 1961(Bangham & Horne, 1964). Later in 1965, liposomes were first described as cell membrane designs as they were made up of the same material as cell membranes (Rendi, 1965). They are microscopic spherical vesicles composed of phospholipids (amphiphilic molecules with a hydrophilic head and a hydrophobic tail). They are formed spontaneously in various sizes when specific lipids are hydrated in aqueous media. The hydrophilic part of phospholipids mainly consists of phosphoric acid bound to water-soluble molecules. In contrast, the hydrophobic part is two fatty acid chains with 10-24 carbon atoms and 0-6 double bonds in each chain. The hydrophilic/ hydrophobic interactions between lipid-lipid and lipid-water molecules lead to the formation of bilayered vesicles to achieve a thermodynamic equilibrium in the aqueous phase.

Liposomes can be employed as drug-targeting molecules in humans; phospholipids are the main components of the cell membrane; liposomes possess excellent biocompatibility and amphiphilic properties (Li et al., 2014). In 1974, liposomes were identified as immunologically effective entities. In the same year, the first injectable liposome product (amphotericin B formulation) was approved for clinical use (Allison & Gregoriadis, 1974) (He, Lu, Qi, Zhu, Chen & Wu, 2019). The lipid bilayer composition of liposomes can be modulated to obtain desirable properties, like a prolonged circulatory half-life, the ability to form a complex with nucleic acids, and the capacity to deliver encapsulated contents to the cytosol (Bangham, 1993). This biocompatibility of liposomes provides a wide range of applications. The most notable application of liposomes is in drug delivery (as they can be filled with the component to be

delivered) and is still undergoing rigorous research for improvement. In medicine, liposomes are used for the smart delivery of drugs, vaccine adjuvants, and signal enhancers for improved diagnosis (Daraee, Etemadi, Kouhi, Alimirzalu & Akbarzadeh, 2016). The liposome's stability in manufacturing, storing, and delivering the drug molecule is critical to the therapeutic effect. An active molecule's physical stability and chemical integrity are preserved throughout its development and storage with a stable dosage form (Yadav et al., 2017). To demonstrate the in vivo activity of liposome-entrapped drugs, cytosine arabinoside was first used, and a significant increase in the survival rate of mice bearing leukemia L1210 was observed (Mayhew Lazo, Vail, King & Green, 1984).

The delivery of the drug molecules to the site of action occurs by the fusion of lipid bilayers with other bilayers of the cell (cell membrane). This adsorption of liposomes on the cell surface membrane is followed by engulfment and internalization into the cell. Lateral diffusion and intermingling of lipids result in the direct delivery of liposomal contents in the cell cytoplasm. Due to the similarity of liposomal lipid membrane with cell membrane phospholipids, lipid transfer proteins in the cell membrane easily recognize liposomes and cause lipid exchange. For example, cancer cells consume large amounts of fats to fill the requirement of rapid growth; they acknowledge liposomes (loaded with anti-cancer drugs) as a potential source of nutrition. When liposomes target cancer cells, they get absorbed. Once the anti-cancer drugs are released from the Liposome into the site, cancer cells are killed by the drug.

Liposomes also have an excellent emulsifying property to stabilize the emulsions used in the drug coating to provide hydrophilicity to hydrophobic drugs (Bozzuto & Molinari, 2015). Liposomes can also carry biomolecules associated with their surfaces as ligands. Liposomes are also used in cosmetics as penetration enhancers, solubilizers, and support matrices for various ingredients (ibid). Liposomes have many advantages; for example, they provide a larger drug payload per particle. They can contain multiple hydrophilic and hydrophobic diagnostic or therapeutic agents. They protect the encapsulated agents from metabolic processes. They have been proven to have favorable in vivo pharmacokinetic properties (that is why they are considered attractive vehicles for anti-cancer drug delivery).

Literature Review

In recent years, scientometrics and bibliometrics analyses have been widely used in many domains to track research trends in exploring the subject development, authors' interest, and the involvement of the research institute or funding agency that promotes the research/er of the field. Few bibliometric and scientometrics studies have been done on liposomes as well as on drug delivery as follows:

Sharma (2021) evaluated 32855 liposome research publications for 2011- 2020 of the Scopus database. The number of publications grew globally by an average of 2.76% each year, from 2907 in 2011 to 3695 in 2020. China, India, and the United States were the most productive countries. Researchers from the Chinese Ministry of Education, the CNRS, and the Chinese Academy of Sciences published the most articles. Biochemistry, genetics, and molecular biology are the fields with the most publications. Most articles were published during this time in the *Journal of Controlled Release*. Hideyoshi Harashima from Hokkaido University in Japan was the author with the most papers. Ale Ebrahim, Zamani Pedram and Ale Ebrahim (2020) performed a bibliometric study on drug delivery research from 1974 to 2019.

Data have been gathered from the Scopus database and analyzed utilizing network analysis

of research outputs to evaluate trends. The study examined the document citations, funding organization, themes, and keywords. The discovered publication trend indicates that systemic drug delivery research is a hotspot. The study also outlines the current state and potential future research directions on systemic drug delivery. Robert, Wilson, Venuta, Ferrari and Arreto (2017) have examined the research productivity of drug delivery based on the web of science between 1974 and 2015. For three decades (1974-2003), the rise of papers on drug delivery publications and literature exploded four times between 2004 and 2015. During the first few decades, industrialized countries such as the USA, UK, Germany, Japan, Italy, France, and Canada were the most productive. Still, in 2014-2015, China, India, and South Korea ranked first, third, and fourth among those countries. *Journal of Controlled Release, Advanced Drug Delivery Reviews,* and *International Journal of Pharmaceutics* published approximately one-fifth of the drug delivery research in 2014-2015. Over the past 15 years, the number of journals targeted by drug delivery research grew nearly 2.4 times.

Zhou and Zhao (2015) analyzed the scientific output of global liposome research between 1995 and 2014 using the Web of Science database. The study of liposomes has advanced significantly during the last two decades. *The International Journal of Pharmaceutics* published most liposome articles during the study period. The USA, Western Europe, and Asia are home to significant author clusters and research areas. The most considerable number of papers in liposome research were produced in the USA. The three universities with the most papers on liposomes were Osaka University (Japan), Kyoto University (Japan), and the University of Texas (USA). Van Rooijen N (Netherlands) was a significant contributor to liposome research. Most papers in the field of liposome study are related to chemistry. Keyword analysis reveals that Gene, drug delivery, cells, and cancer were the main research areas during the study period. Nanotechnology, medication delivery, small interfering RNA, and cancer treatment received incredible attention during the study period, perhaps indicating future research tendencies.

The literature review proves that scientometric research has been done on Liposomes and drug delivery separately; however, little effort has been made to systematically collect bibliometric data on liposomes as drug delivery for evaluating and examining the scientific literature. The present study aims to analyze the publication growth trends, Language research, type of research, most cited research papers, most relevant cited references, current research trends, top countries, top funding agencies, top organizations, the most prolific authors, and the most productive journals publishing research in the field based on the data downloaded from the web of science.

Research Question

What are the scientometric outcomes of research done on liposomes as drug delivery?

Therefore, the present study applied a scientometric approach to evaluate and map the research productivity on Liposome as drug delivery based on literature indexed in the Web of Science. More Specifically, this paper aims to explore publications growth and trends, most relevant sources, evaluate top authors, organizations, and countries, and analyze the most cited research papers, references, most used author keywords, and explore research themes.

Materials and Methods

Methods: This study used the Scientometric method to analyze global Liposomes as drug delivery research publications using the Web of Science. Bibliometrics uses statistical

approaches to analyze documents such as books, articles, reports, and other publications. These approaches are frequently utilized in library and information science, and Scientometric is a branch of bibliometrics concerned with analyzing scientific publications. The Scientometric study is a quantitative method used to examine research trends in a particular domain. Bibliographic data of this research was retrieved from the Web of Science database, and analysis focused on yearly research growth and development, most reverent source, organization and authors, most crucial research theme, and country collaboration, etc.

Search Query: To retrieve the topic's bibliographic data, the following search query was run in the search box of the Web of Science database.

- TI= TITLE: (liposomes) AND TITLE: (Drug delivery)
- Timespan: 1980-2021
- Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC.

Inclusion/Exclusion (Screening): A total of 35 publications (11 duplicate publications and 24 publications by screening the title and abstract) were excluded from the initial search result of 664 publications**.**

Time Span: The data extracted from 1980 to 2021 since, as per the search strategy, the first article on Liposome as drug delivery appeared on the Web of Science in 1980.

Date of data extraction: The present study's targeted data was collected and downloaded from the Web of Science database used at Imam Abdulrahman Bin Faisal University on 20th February 2021. Some research publications (629) were selected for download (Figure 1).

Data Analysis: A highly relevant literature of a total of 629 publications was downloaded and performed using various tools and software, including Bibexcel (Persson & Danell, 2009), RStudio (Biblioshiny), and VOSviewer (van Eck & Waltman, 2010).

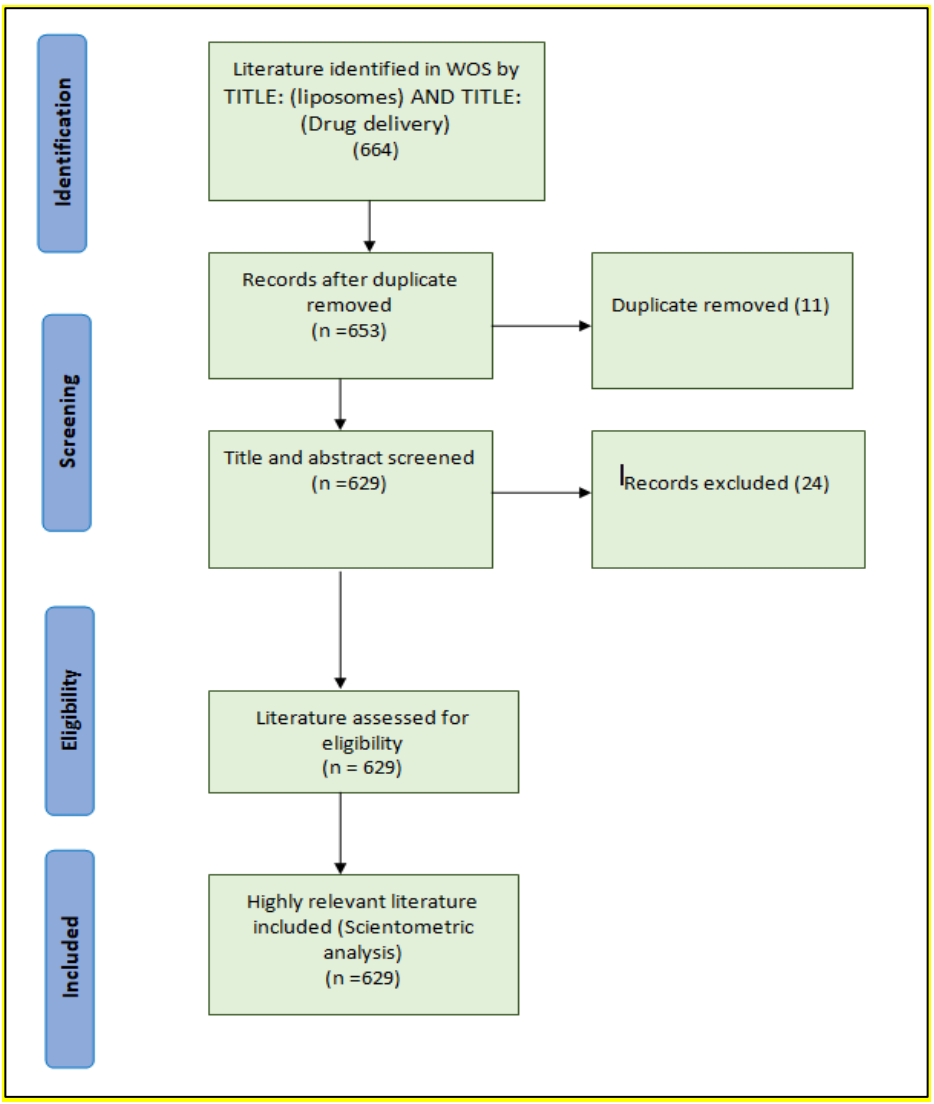


Figure 1: PRISMA Flow Diagram for Scientometric Analysis on Liposomes as a Drug Delivery

Result

Analysis of Results

The collected data spans from 1980 to 2021 from 270 sources, including journals, books, and conference proceedings. With the abovementioned strategy, the total data in this period comprises 629 documents. The average years from publication for each document is found to be 11.1. Each document received approximately 39.37 citations. The average citation of each document per year is 3.507, and the Total references of these documents sum up to 20272.

Languages

Research on the use of liposomes for drug delivery has been conducted in five different languages, with 99% of work done in English, represented in Table 1. 623 English documents received 24740 combined citations. Other languages are French, Chinese, Russian, and Portuguese with 2, 2, 1, and 1 paper. It is noticeable from the analysis that 1 Russian document has received 12 citations, which is more than the citations for 2 French and Chinese documents.

Table 1
Language of Research Work Published on the Use of Liposomes for Drug Delivery

Rank	Language	NP	TC	Citation sum within h-core	h-index
1	English	623	24740	14936	78
2	French	2	8	8	1
3	Chinese	2	4	4	1
4	Russian	1	12	12	1
5	Portuguese	1	0	0	0

NP=Number of Publications, TC=Total citations

Annual Research Trends in Liposomes from 1980 To 2021

Table 2 shows that from 1980 to 2004, few documents were published yearly, ranging from 1 to 14, with an average of 5.72 papers each year. And it was not a gradual increase; there was a fluctuation in the number of publications, for example, in 1986 there was 1 document, and the number rose to 4 papers in 1987 before it went down to 2 in 1988, the further number surged to 8 in 1989. From 2005 onwards, there was a slow and steady rise in publications, with the highest number of publications reaching 49 in 2018 and 2019. The lowest publication recorded is 01 document in 1980, 1981, 1985, and 1986; the document published in 85 has no citation. The highest number of total citations in 2004 was obtained for 34 publications in 2011. Documents published in 1994, 1999, 2018, and 2019 are widely used compared to other documents in the last 180 days.

Overall, the outputs are almost constant this decade, with some reviews and new findings on the use of liposomes in drug delivery. Nevertheless, the average number of publications has not reached a high level, suggesting that this field still has much scope for further detailed research and needs attention.

Table 2
Annual Research Trends on the Use of Liposomes for Drug Delivery

Year	NP	TC	Citation sum within h-core	h-index	U1
1980	1	351	351	1	0
1981	1	42	42	1	0
1982	5	691	691	5	24
1983	5	321	321	4	24
1984	2	58	58	1	0
1985	1	0	0	0	0
1986	1	39	39	1	0
1987	4	21	21	2	7
1988	2	39	39	2	0
1989	8	372	372	7	3
1990	5	14	14	2	24
1991	6	71	66	4	13
1992	4	438	438	4	7
1993	8	361	352	5	3
1994	7	973	971	5	32

Year	NP	TC	Citation sum within h-core	h-index	U1
1995	5	557	556	3	24
1996	9	510	501	5	4
1997	8	1192	1187	5	3
1998	6	276	270	3	13
1999	7	381	378	4	32
2000	10	785	784	8	2
2001	11	320	315	7	17
2002	14	566	565	10	8
2003	8	138	137	3	3
2004	5	268	267	3	24
2005	15	927	923	11	3
2006	12	631	631	11	14
2007	20	978	965	12	5
2008	15	869	858	10	3
2009	16	1545	1538	11	9
2010	15	1055	1041	11	3
2011	34	2004	1899	20	0
2012	33	1949	1875	22	1
2013	37	1114	1028	19	3
2014	38	1139	1012	20	0
2015	31	746	657	15	2
2016	38	939	802	17	0
2017	43	798	660	15	0
2018	49	758	515	16	33
2019	49	471	273	12	33
2020	37	55	26	5	3
2021	3	2	2	1	20

U1=Usage counts in the last 180 days

Type of Documents

The data shows in Table 3 that the research published on “Liposome in drug delivery” comprises research articles, book chapters, editorials, conference papers, reviews, etc. The highest percentage of publications (395) are in articles, followed by 95 meeting abstracts, 86 reviews, and 21 proceedings papers. Fourteen articles in proceedings, nine editorial materials, four corrections, two reviews, and a book chapter, while few publications are in the form of notes, Articles, early access, and book reviews; this result agrees with (Rahaman, Kumar, Ansari & Rahman, 2021; Rahaman, Ansari, Kumar & Shah, 2022).

Table 3
Documents Type on the Use of Liposomes for Drug Delivery

Rank	Type of documents	NP	TC	Citation sum within h-core	h-index
1	Article	395	14363	8048	64
2	Meeting Abstract	95	53	12	3
3	Review	86	9055	8354	43
4	Proceedings Paper	21	88	72	4
5	Article; Proceedings Paper	14	614	594	12
6	Editorial Material	9	381	378	7
7	Correction	4	1	1	1
8	Review: Book Chapter	2	7	7	1
9	Note	1	202	202	1
10	Article: Early Access	1	0	0	0
11	Book Review	1	0	0	0

Relevant Sources

Studies regarding liposomes and their use as drug-delivery agents are published in various journals. Table 4 shows the ranking of journals according to the number of publications (NP) in the data set, as well as total citations (TC), h-index, g-index, m-index, and publishing year start (PY start) of journals also mentioned. The Journal of Controlled Release, which first published the work on the Liposome as drug delivery in 1990, is the most prolific journal with the highest number of publications (45 NP) and highest TC, i.e., 3063; besides, it has the highest H-index of 27. Journal of Controlled Release publishes cutting-edge research in delivery science and technology. This paper grabbed a lot of attention across the globe and received the highest number of citations. The second most productive journal is the International Journal of Pharmaceutics, with 30 publications and 1587 TC acquiring an h-index of 17. International Journal of Pharmaceutics is a journal that publishes articles focused on natural and clinical sciences and encourages submitting papers that contain original research work. Abstracts of Papers of the American Chemical Society has published many documents but has not received enough citations and has the least TC (6) and least H-index of 1. Journal of Drug Targeting is another impactful journal with 16 NP, 655 TC, and 13 as h-index. Journal of Drug Targeting aims to publish work that covers molecular biology research methods and protocols.

Though it has only 10 NP, the European Journal of Pharmaceutical Sciences has received good citations, i.e., 747 and 9 as h-index. European Journal of Pharmaceutical Sciences publishes all aspects of the pharmaceutical sciences, emphasizing conceptual novelty and scientific quality. Biochemica Et Biophysica Acta is the journal with the least number of publications. However, before all other journals, it published the first document on the topic in 1983.

Table 4
The Top 20 Sources on the Use of Liposomes for Drug Delivery

Rank	Source	NP	TC	h-index	g-index	m-index	PY-start
1	Journal of Controlled Release	45	3063	27	45	0.84	1990
2	International Journal of Pharmaceutics	30	1587	17	30	0.61	1994
3	Abstracts of Papers of the American Chemical Society	28	6	1	2	0.03	1990
4	Journal of Drug Targeting	16	655	13	16	0.46	1994
5	Journal of Liposome Research	15	257	9	15	0.36	1997
6	Colloids and Surfaces B-Biointerfaces	13	436	7	13	0.27	1996
7	International Journal of Nanomedicine	13	507	9	13	0.56	2006
8	European Journal of Pharmaceutical Sciences	10	747	9	10	0.43	2001
9	European Journal of Pharmaceutics and Biopharmaceutics	10	315	9	10	0.60	2007
10	Drug Delivery	8	239	7	8	0.54	2009
11	Pharmaceutical Research	8	418	8	8	0.27	1992
12	Pharmaceutics	8	46	4	6	0.67	2016
13	Advanced Drug Delivery Reviews	7	858	6	7	0.24	1997
14	Biomaterials	7	649	7	7	0.39	2004
15	Chemistry and Physics of Lipids	7	373	6	7	0.23	1996
16	Journal of Drug Delivery Science and Technology	6	71	5	6	0.36	2008
17	Journal of Pharmaceutical Sciences	6	162	5	6	0.16	1991
18	Soft Matter	6	75	4	6	0.31	2009
19	Biochimica et Biophysica Acta	5	502	4	5	0.10	1983
20	Expert Opinion on Drug Delivery	5	107	4	5		2008

Authors

The total number of authors is 2417, and they have appeared 3116 times. Thirty authors have single-authored documents to their account, while 2387 are authors of multi-authored papers.

Prolific Authors of Liposomes for Drug Delivery Research

Gregoriadis G. is the fortunate 1st ranked author regarding total citations (TC), obtaining 921 TC acquiring H-index (6), with seven publications indicating the significance of his work in the field. Gregoriadis made the first move towards the use of liposomes in drug delivery. His work led to the clinical approval of liposome application (Gregoriadis & Perrie, 2010). Gregoriadis was the first one to start the work in the field. Liu Y is another prolific author to

work in this area. Liu Y has the highest h-index (10), g-index (15), m-index (1.111), and NP (15), though he started work very late in the field (i.e., in 2013). Liu Y has worked on using liposomes as drug delivery in anti-cancer therapy. The next significant author in this discipline is Koning GA with eight h-index and g-index and TC 521 for eight publications. Koning's work mainly uses liposomes to improve drug delivery in solid tumors. Wang Z is a recent notable author in the field who started work in 2015, has seven publications with 121 TC, and has acquired an h-index of 6, as shown in Table 5.

Table 5
Prolific Authors of Liposomes for Drug Delivery Research

Rank	Author	h-index	g-index	m-index	TC	NP	PY-start
1	Liu Y	10	15	1.111	342	15	2013
2	Koning GA	8	8	0.667	521	8	2010
3	Zhang L	6	8	0.545	164	8	2011
4	Gregoriadis G	6	7	0.15	921	7	1982
5	Huang SL	3	7	0.143	339	7	2001
6	Li X	6	7	0.545	174	7	2011
7	Liu X	4	7	0.4	81	7	2012
8	Wang X	6	7	0.6	222	7	2012
9	Wang Z	6	7	0.857	121	7	2015
10	Chen H	4	6	0.333	163	6	2010
11	Chen J	6	6	0.6	108	6	2012
12	Li J	5	6	0.455	144	6	2011
13	Sun X	5	6	0.417	141	6	2010
14	Ten Hagen TLM	6	6	0.5	453	6	2010
15	Wang J	4	6	0.235	153	6	2005
16	Wang Y	4	5	0.364	32	6	2011
17	Zhang Q	6	6	0.6	426	6	2012
18	Barenholz Y	4	5	0.103	481	5	1983
19	De Smet M	5	5	0.455	369	5	2011
20	Eggermont AMM	5	5	0.417	430	5	2010

Author Collaboration

Among 2417 documents, 35 are single-authored documents. Analytically, there are 3.84 authors per document. Data analysis implies that there are 0.26 documents per author. It also means that 4.95 co-authors per document suggest more collaborative work in this research area: a collaboration index of 4.02. Trends in author collaborations show researchers in the field of liposomes as drug delivery prefer collaborative research.

Co-citation Network of Cited Authors

Figure 2 represents the most locally cited authors and co-citations. Each dot represents an author; the size of the dots varies in proportion to the number of citations. Lines between dots show the link between authors, reflecting that they have been co-cited. The number of lines

attached to a dot represents the link strength of that author. Therefore, with the help of link clustering and multidimensional scaling techniques, mapping the structure of specialized research areas can be done with co-citation network analysis. Co-citation was selected from 'types of analysis,' and cited authors selected from a 'unit of analysis, ' a complete method used for calculation, and a minimum (25) number of citations of an author considered for analysis. Of the (14313) authors, (50) meet the thresholds. For each (50) author, the total strength of the co-citation links with the other authors will be calculated. The authors with the greatest total link strength will be selected. Full item found (50), cluster (4), links (1043), and total link strength (14440).

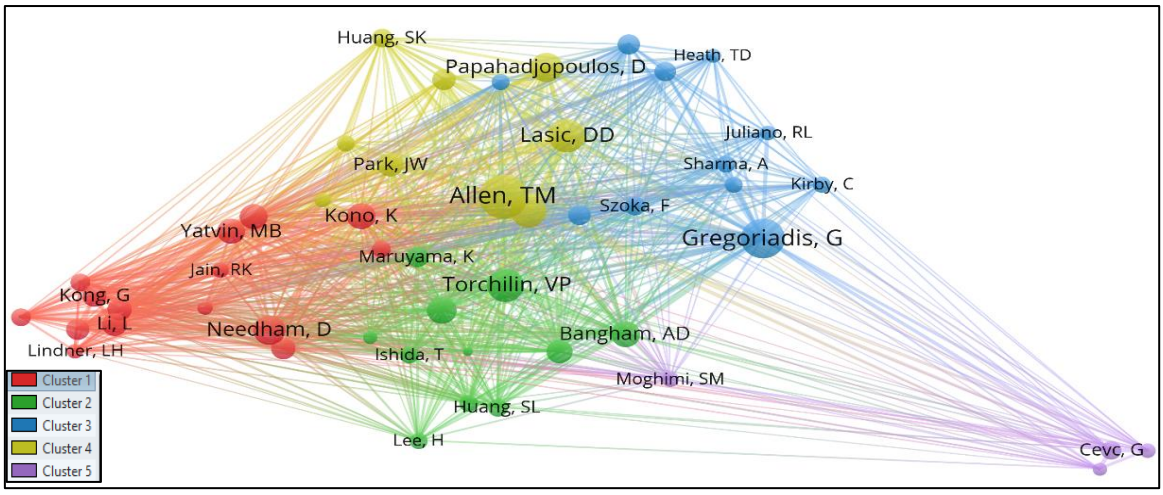


Figure 2: Mapping Co-citation of Cited Authors of Liposome

Cluster 1 consists of 15 co-cations of cited authors (most prominent are Needham D, Kono K, Drummond DC, Yatvin MB, Li L, Maeda H, Kong G, Tagami T, De Smet M, Hossain M, Koning GA). **Cluster 2** represents 11 co-citations of cited authors (Torchilin VP, Barenholz Y, Bangham AD, Klibanov AL, Maruyama K, Huang SL, Ishida T, Schroeder A, Lee H, Immordino ML, Takeuchi H). The majority of dots in the same cluster are closer, which means that the authors with similar research interests are closer in the network.

Cluster 3 constitutes 11 co-cited authors (Gregoriadis G, Connor J, Mayer LD, Straubinger RM, Szoka F, Sharma A, Alving CR, Lee RJ, Kirby C). Gregoriadis G is in 2nd position concerning the number of citations, has received 202 citations, and has the second-highest link strength, i.e., 1862. Gregoriadis' work was a pioneering step in this field. His first work on liposomes, published in 1971, was about the entrapment of enzymes in liposomes. His work focuses on using liposomes as carriers, with his most recent work titled "Liposomology: Delivering the Message," published in 2018. **Cluster 4** designates 9 co-citations (Allen TM, Lasic DD, Gabizon A, Papahadjopoulos D, Park JW, Woodle MC, Huang SK, Gabizon AA, Haran G). Allen TM received the highest number of citations, i.e., 205, and has the highest link strengths, i.e., 2244.

Cluster 5 denoted 4 co-cited authors (Cevc G, Moghimi SM, Mezei M, Touitou E).

Most Cited Documents of Liposomes

Table 6 shows the top 10 most cited research papers on liposomes. The top ten listed cited papers ranged between 340 and 743 citations. The article entitled 'Liposomes and

nanoparticles: nanosized vehicles for drug delivery in cancer' by Malma, Loizidou and Seifalian (2009) was the most cited research paper on liposomes with 743 citations, followed by 'Liposomes in drug delivery: progress and limitations' by Sharma and Sharma (1997) with 699 citations, 'Engineering liposomes for drug delivery: progress and problems' by Gregoriadis (1995) with 478 citations, 'Liposomes: from a clinically established drug delivery system to a nanoparticle platform for theragnostic nanomedicine' by Al-Jamal and Kostarelos (2011) with 441 citations and 'Long-circulating (sterically stabilized) liposomes for targeted drug delivery by Allen (1994), with 394 citations. The article 'Pulsed-high intensity focused ultrasound, and low-temperature sensitive liposomes for enhanced targeted drug delivery and antitumor effect by Dromi (2007) was the least cited among the top ten cited papers with 340 citations. According to the Web of Science database, the article entitled 'Liposomes: from a clinically established drug delivery system to a nanoparticle platform for theragnostic nanomedicine' by Al-Jamal and Kostarelos (2011) was highly used amongst the top ten cited papers 14 times in the last 180 days (U1), while used 572 times since 2013 (U2).

Table 6
Top 10 Most Globally Cited Research Papers on Liposomes

Rank	Title	TC	Author	Year	Journal	U1	U2	TC /Year	NTC
1	Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer(Malam, Loizidou, and Seifalian 2009)	743	Malam, Y	2009	*Trends in Pharmacological Sciences*	13	162	57.15	7.69
2	Liposomes in drug delivery: progress and limitations (Sharma and Sharma 1997)	699	Sharma, A	1997	*International Journal of Pharmaceutics*	7	236	27.96	4.69
3	Engineering liposomes for drug delivery: progress and problems (G Gregoriadis 1995)	478	Gregoriadis, G	1995	*Trends in Biotechnology*	5	137	17.70	4.29
4	Liposomes: from a clinically established drug delivery system to a nanoparticle platform for theragnostic nanomedicine (Al-Jamal and Kostarelos,2011)	441	Al-Jamal and Kostarelos	2011	*Accounts of Chemical Research*	14	572	40.09	7.48
5	Long-circulating (sterically stabilized) liposomes for targeted drug-delivery (T M Allen 1994)	394	Allen, TM	1994	*Trends in Pharmacological Sciences*	1	68	14.07	2.83
6	Liposomes and skin: from drug delivery to model membranes (El Maghraby, Barry, and Williams 2008)	377	El, Maghraby, GM	2008	*European Journal of Pharmaceutical Sciences*	4	79	26.93	6.51
7	Current status of ph.-sensitive liposomes in drug delivery (Drummond, Zignani & Leroux, 2000)	370	Drummond, DC	2000	*Progress in Lipid Research*	3	93	16.82	4.71

Rank	Title	TC	Author	Year	Journal	U1	U2	TC /Year	NTC
8	Liposomes - a selective drug delivery system for the topical route of administration .1. Lotion dosage form (Mezei & Gulasekharam, 1980)	351	Mezei,M	1980	*Life Sciences*	0	20	8.36	1.00
9	Liposomes and niosomes as topical drug carriers - dermal and transdermal drug-delivery (Schreier & Bouwstra, 1994)	341	Schreier, H	1994	*Journal of Controlled Release*	1	102	12.18	2.45
10	Pulsed-high intensity focused ultrasound and low temperature sensitive liposomes for enhanced targeted drug delivery and antitumor effect (Dromi et al. 2007)	340	Dromi et al.	2007	*Clinical Cancer Research*	9	138	22.67	6.95

U1=Usage counts in last 180 days U2= Usage counts since 2013 NTC= Normalized total citation

Reference Documents

The analyses have been done to identify the top cited references and co-citations of cited references in the liposomes drug delivery research.

Mapping of Co-Citation of Cited References

To map the co-citations of cited references, co-citations were selected from 'types of analysis.' They cited references chosen from a 'unit of analysis, a complete method used for calculation. A minimum (20) citations of cited references have been considered for analysis, and out of the (220237) cited references, 18 met the thresholds. There were 18 items, 3 clusters, 142 links, 142, and 601 link strength. Figure 2 shows a map of bibliographic coupling based on the cited source with these 18 cited references. Each circle represents a source (journal article or conference paper), and the circle size indicates the source activity. The larger the circle, the more active the source is in the field and vice versa. The distance between two circles represents the degree of association between two sources. The shorter the distance, the stronger the correlation between the sources and vice versa. The thickness of the links between the sources indicates the strength of the co-citation relationship.

Therefore, cited references with the greatest total link strength will be selected. Strong co-citation between sources generates clusters. Clusters 1, 2, and 3 represent 8, 6, and 4 sources. Cluster 1 includes crucial articles published by Klibanov, Maruyama, Torchilin and Huang (1990), Allen, Theresa and Cullis (2013), and Bangham, Standish and Watkins (1965). A total of 6 sources are falling in cluster 2. In science, the article under Cluster 3 published by Yatvin, Weinstein, Dennis and Blumenthal in 1978, has the highest link strength (109). Cluster 3 includes two articles by author Needham D, from which the one published in 2000 in Cancer Research has a higher link strength (96).

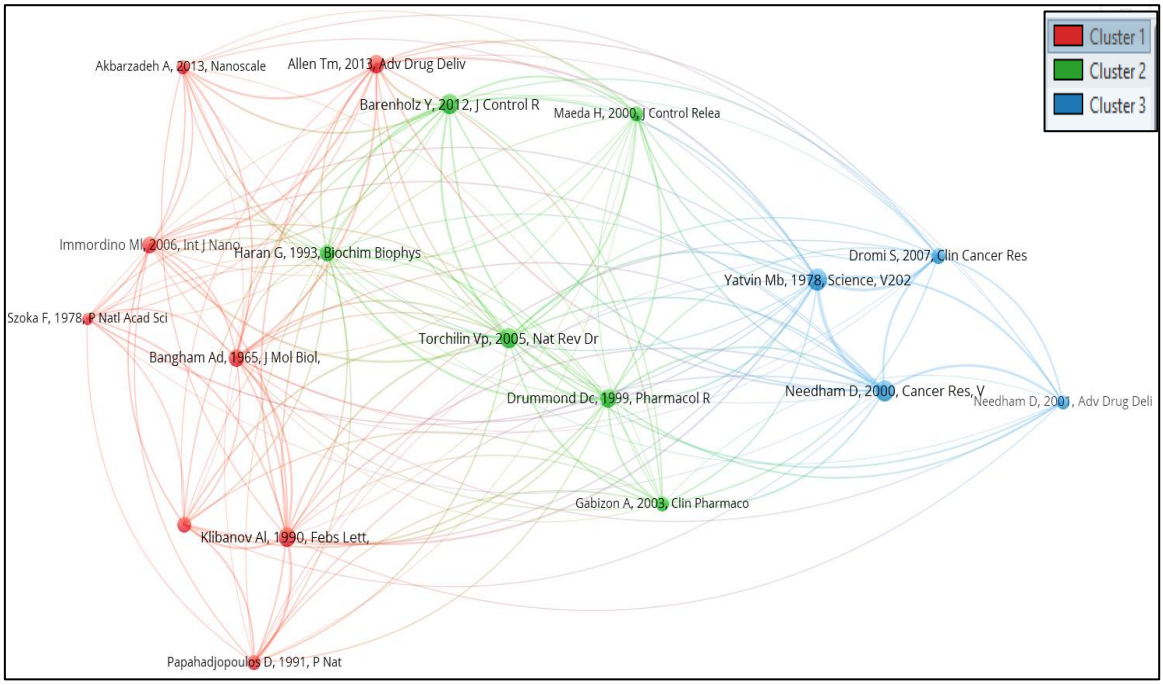


Figure 3: Visualizing Co-Citation of Cited References

Top 10 cited references (refer to VOSviewer visualization of cited reference)

The top 10 cited papers are arranged in Table 8, which lists the details of the most influential papers, including author, type, year, and citation. "Recent advances with liposomes as pharmaceutical carriers" by Torchilin (2005) received the highest citations (53), followed by "Membrane models with phospholipids" by Bangham et al. (1965), with 44 citations. From Table (7), five publications are articles, and 5 are reviews. The top three cited publications are all reviews and high-cited papers. Furthermore, two study liposomes as carriers, widely investigated from basic theories, methods, and applications. Besides, the top 10 most cited papers were published from 1965 to 2013. Furthermore, 3 of them are single-authored documents, while the rest have more than one author, indicating that the cooperation of authors plays a crucial role in academic research.

Table 7
Top 10 Most Cited References in Liposomes

Rank	Title	Cited References	Type	TC
1	Recent advances with liposomes as pharmaceutical carriers (Torchilin, 2005)	Torchilin Vp, 2005, Nat Rev Drug Discov, V4, P145, Doi 10.1038/Nrd1632	Review	53
2	Diffusion of univalent ions across the lamellae of swollen phospholipids (Bangham, Standish & Watkins, 1965)	Bangham Ad, 1965, J Mol Biol, V13, P238, Doi 10.1016/S0022-2836(65)80093-6	Review	44
3	Liposomal drug delivery systems: From concept to clinical applications (Theresa M Allen and Cullis 2013)	Allen Tm, 2013, Adv Drug Deliver Rev, V65, P36, Doi 10.1016/J.Addr.2012.09.037	Review	43
4	Design of liposomes for enhanced local release of drugs by hyperthermia	Yatvin Mb, 1978, Science, V202, P1290, Doi 10.1126/Science.364652	Article	41

Rank	Title	Cited References	Type	TC
	(Yatvin et al. 1978)			
5	A new temperature-sensitive liposome for use with mild hyperthermia: Characterization and testing in a human tumor xenograft model(Needham, Anyarambhatla, Kong & Dewhirs, 2000)	Http://Www.Scopus.Com/Inward/Record.Url?Eid=2-S2.0-0034161921&Partnerid=MN8TOARS	Article	37
6	Doxil®--the first FDA-approved nano-drug: lessons learned (Barenholz, 2012)	Barenholz Y, 2012, J Control Release, V160, P117, Doi 10.1016/J.Jconrel.2012.03.020	Review	36
7	Amphipathic polyethyleneglycols effectively prolong the circulation time of liposomes (Klibanov, et al. 1990)	Klibanov Al, 1990, Febs Lett, V268, P235, Doi 10.1016/0014-5793(90)81016-H	Article	29
8	Sterically stabilized liposomes: improvements in pharmacokinetics and antitumor therapeutic efficacy (Papahadjopoulos, et al. 1991)	Papahadjopoulos D, 1991, P Natl Acad Sci USA, V88, P11460, Doi 10.1073/Pnas.88.24.11460	Article	27
9	Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation (Szoka Jr & Papahadjopoulos, 1978)	Szoka F, 1978, P Natl Acad Sci Usa, V75, P4194, Doi 10.1073/Pnas.75.9.4194	Article	27
10	Optimizing liposomes for delivery of chemotherapeutic agents to solid tumors (Drummond, Meyer, Hong, Kirpotin & Papahadjopoulos, 1999)	Drummond Dc, 1999, Pharmacol Rev, V51, P691	Review	26

Document Contents

The research trend was identified by analyzing keywords from the evidence of Scopus-based procured documents (on Liposome as drug delivery research). It has been found that the authors assign 1790 indexed keywords (Keyword Plus) and 1332 keywords. However, the analysis was conducted to identify the research trend by considering author keywords. Keyword Plus gives random keywords, whereas author keywords are more relevant to the topic.

Keyword analysis by Co-occurrence of Author Keywords

Co-occurrence selected from "types of analysis" and author keywords selected from a "unit of analysis" Counting method: total counting/Fractional counting. Minimum (5) occurrences of keywords considered for analysis. Out of the (1251) keywords, (34) meet the thresholds. For each of the (34) keywords, the total strength of the co-occurrence links with the other keywords will be calculated. The keywords with the greatest total link strength will be selected. Full item found (34), cluster (9), links (151), and total link strength (419). Ansari, Khan, Omar, El-Wakeel and Rahaman (2021) conducted a similar type of author keyword analysis in Anthropometric measurement and Rahaman, Ansari, Kumar and Shah (2022) in solid waste management.

Keyword analysis displays that the author's keyword "liposome" is the frequently appearing

keyword with 231 occurrences, while the word "Drug Delivery" is next in line with 89 occurrences (Figure 4). The next author's keywords are "doxorubicin," with 28 occurrences and 44 link strength. A few keywords usually appearing are technically similar, such as “oral drug delivery,” “drug delivery system,” “targeted delivery,” and “targeted drug delivery.” Close observation of the analysis displays similar words like “drug release” and “triggered release.” “Temperature-sensitive liposome” and “doxorubicin” are other keywords that appear regularly. All these keywords suggest that liposome drug delivery is a hot spot in drug delivery research. A few keywords that appeared here seem insignificant to this particular topic, such as “gene therapy” and “pegylation,” but an in-depth study links these keywords and the area of research.

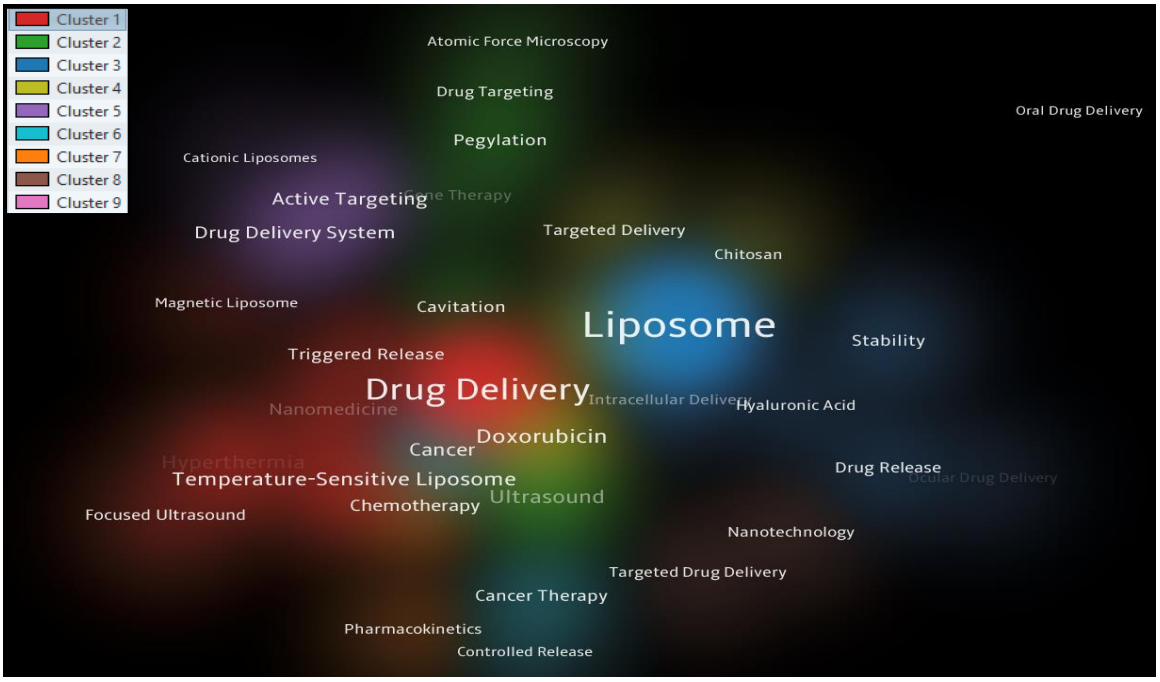


Figure 4: Analysis of Author Keyword Through Vosviewer

Country and Affiliations

The following analyses have been done with the help of RStudio’s Biblioshiny software to identify and recognize the most contributing countries and the most productive institutions in liposome drug delivery research. The following results have been observed.

Productive Countries

Table 8 illustrates the highest output of articles on “liposomes as drug delivery” in the top 20 countries. Based on this analysis, publications on Liposome as drug delivery come mainly from the USA, with 181 records representing 28.77% of total documents. A similar type of results was reported by Rahaman, Kumar, and Shah (2021). The People's Republic of China was identified as the second leading contributor (104 records), followed by Japan (59 records), Italy (42 records), England (39 records), and the Netherlands (35 records). The USA is the most productive country with the highest citations, i.e., Global Citation Score (GCS) is 7823, and Local Citation Score (LCS) is 211, followed by Italy (GCS=3110, LCS=43), China (GCS=2832, LCS=51), France (GCS=2317, LCS=61), and Netherlands (GCS=1850, LCS=76).

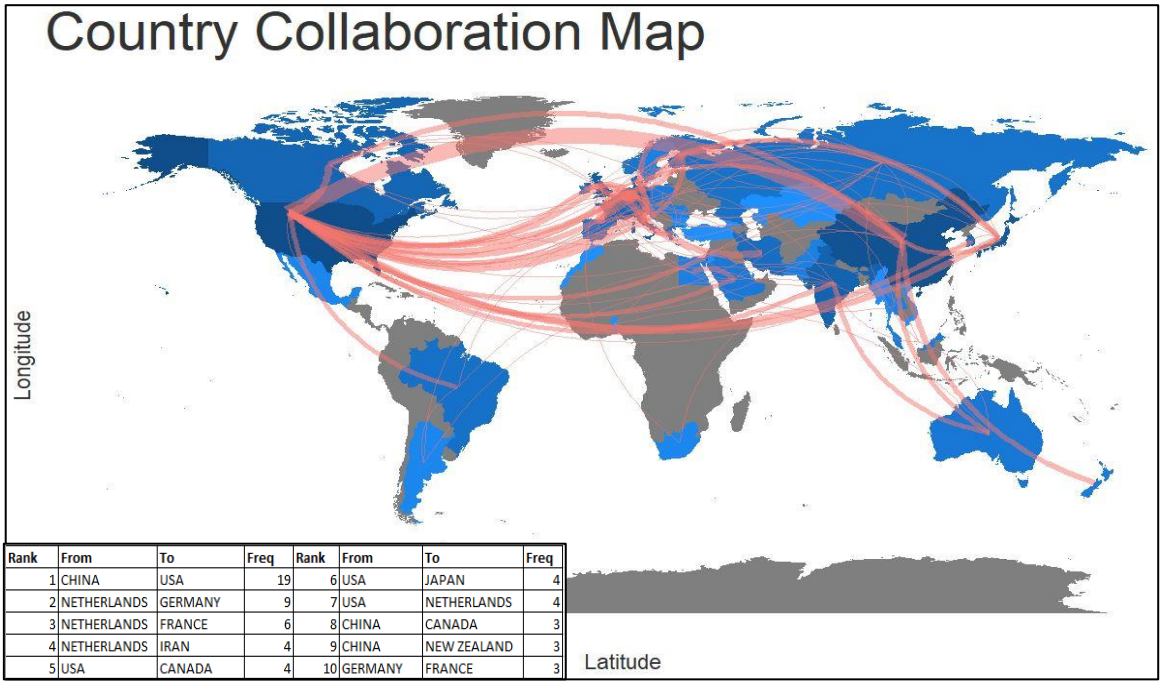
The analysis reveals the USA is the most productive country regarding the frequency of publications and citations. France is in the last position for the number of publications, i.e., 21 records, but its GCS is 2317 (higher than the other six countries in the list), indicating the significance of France's work.

Table 8
Top 20 Most Productive Country on Liposomes

Rank	Countries/Regions	Records out of 629	Percentage of records	LCS	GCS
1	USA	181	28.776	211	7823
2	China	104	16.534	51	2832
3	Japan	59	9.38	22	1153
4	Italy	42	6.677	43	3110
5	England	39	6.2	26	1424
6	Netherlands	35	5.564	76	1850
7	Germany	30	4.769	5	442
8	India	27	4.293	44	1482
9	Canada	24	3.816	14	823
10	France	21	3.339	61	2317
11	Israel	16	2.544	41	774
12	South Korea	15	2.385	23	985
13	Iran	13	2.067	20	551
14	Denmark	12	1.908	21	454
15	Brazil	10	1.59	9	358
16	Finland	10	1.59	9	285
17	Greece	9	1.431	35	697
18	Russia	9	1.431	2	227
19	Spain	8	1.272	7	471
20	Norway	7	1.113	9	291

Countries Collaborations

Figure 5 gives evidence of the top 10 countries' collaboration on liposomes as drug delivery research. Based on the analysis, “The Netherlands,” “China,” and “USA” have the main collaborative networks in the world and consequently are at the forefront of very high production. China emerged as a top collaborator with the USA (19 publications), followed by the Netherlands with Germany (9 publications), the Netherlands with France (6 publications), and the Netherlands with Iran (4 publications). Further, the USA collaborated with three countries, namely Canada (4 publications), Japan (4 publications), Netherlands (4 publications), and succeeded by China’s collaboration with Canada (3 publications) and New Zealand (3 publications). Germany was the least collaborator country among the 10 collaborators, having 3 publications with France.



Rank	From	To	Freq	Rank	From	To	Freq
1	CHINA	USA	19	6	USA	JAPAN	4
2	NETHERLANDS	GERMANY	9	7	USA	NETHERLANDS	4
3	NETHERLANDS	FRANCE	6	8	CHINA	CANADA	3
4	NETHERLANDS	IRAN	4	9	CHINA	NEW ZEALAND	3
5	USA	CANADA	4	10	GERMANY	FRANCE	3

Figure 5: Country Collaboration

Relevant affiliation in the liposomes research

Table 9 shows the top 20 eminent organizations publishing liposome-related papers on drug delivery. Six of the top 20 universities are in China, followed by four in the USA and three in the Netherlands. Though the University of Helsinki Finland has only 9 publications, it has the highest global citation score, i.e., 996. Further, Erasmus MC Netherlands (9 publications) with 692 GCS. Besides, Shenyang Pharmaceutical University China, the University of London UK, and Northwestern University USA have the highest records, i.e., 11 publications. Moreover, surprisingly, two institutes viz. Chinese Academy of Science China and Eindhoven University of Technology Netherlands have identical records (6) with the same GCS (634).

Table 9
Top 20 Most Active Organizations in Liposomes Research

Rank	Organizations	Country	records	% of 629	LCS	GCS
1	Northwestern Univ	USA	11	1.749	9	201
2	Shenyang Pharmaceut Univ	China	11	1.749	8	441
3	Univ London	UK	11	1.749	8	372
4	Univ Calif San Francisco	USA	10	1.59	9	517
5	China Pharmaceut Univ	China	9	1.431	3	161
6	Erasmus Mc	Netherland	9	1.431	35	692
7	Sichuan Univ	China	9	1.431	38	503
8	Univ Helsinki	Finland	9	1.431	48	996
9	Nci, Usa	USA	8	1.272	0	80
10	Southeast Univ	China	8	1.272	3	164
11	Univ Naples Federico Ii	Italy	8	1.272	2	85
12	Hebrew Univ Jerusalem	Israel	7	1.113	4	336

Rank	Organizations	Country	records	% of 629	LCS	GCS
13	Shanghai Jiao Tong Univ	China	7	1.113	2	67
14	Stanford Univ	USA	7	1.113	7	190
15	Teikyo Univ	Japan	7	1.113	4	148
16	Univ Utrecht	Netherland	7	1.113	6	348
17	Chinese Acad Sci	China	6	0.954	23	634
18	Cnrs	France	6	0.954	7	254
19	Dr. Hari Singh Gour Vishwavidyalaya	India	6	0.954	11	493
20	Eindhoven Univ Technol	Netherland	6	0.954	23	634

Influential Funding Agencies

Many financial institutions and agencies identified the production of "Liposome as drug delivery" research. The top 19 highly productive funding agencies are listed in Table 10 concerning the number of studies financed. "National Natural Science Foundation" from China funded 64 research. It bagged the first potions in the top 19 list, followed by "National Institute of Health" from the USA and "United States Department of Health Human Services" which produced 49 records. Most funding agencies are from the USA, China, and Japan. Most of these are government funding agencies.

Table 10
Top 20 Most Influential Funding Agencies of Liposome Research

Rank	Funding Agencies	Records	% of 629
China	National Natural Science Foundation of China NSFC	64	10.175
USA	National Institutes of Health NIH USA	49	7.79
USA	United States Department of Health Human Services	49	7.79
USA	NIH National Cancer Institute NCI	31	4.928
Japan	Ministry of Education Culture Sports Science and Technology Japan MEXT	28	4.452
Japan	Japan Society for The Promotion of Science	23	3.657
Japan	Grants in Aid For Scientific Research Kakenhi	16	2.544
China	National Basic Research Program of China	15	2.385
USA	National Science Foundation NSF	11	1.749
Italy	Ministry of Education Universities and Research MIUR	8	1.272
USA	NIH National Institute of General Medical Sciences NIGMS	8	1.272
Finland	Academy of Finland	7	1.113
Europe	European Union Eu	7	1.113
China	Fundamental Research Funds for The Central Universities	7	1.113
Brazil	National Council for Scientific and Technological Development CNPQ	6	0.954
China	National High Technology Research and Development Program of China	6	0.954
USA	NIH National Heart Lung Blood Institute NHLBI	6	0.954
USA	United States Department of Defense	6	0.954
Brazil	Capes	5	0.795

Thematic Evolution author keywords

Figure 6 demonstrates the thematic evolution of author keywords in three time slices (1980-2009), 2010-2016, and 2017–2021). Biblioshiny packages created this thematic evolution of author keywords. Liposomes, drug delivery, and cationic Liposome are the most important author keywords appearing in all the three-time slices. Drug delivery, drug targeting, cancer therapy, cationic liposomes, release, and targeted drug delivery are the most popular research themes in the first stages (1980-2009). Nanotechnology, cancer, ultrasound, cellular uptake, pharmacokinetics, chitosan, and pegylation were the most popular research themes in the second stage (2010–2016). The new topics recently gained popularity in liposomes as drug delivery research include permeability, ocular drug delivery, Chemotherapy, Cancer therapy, Nanoparticles, Hypoxia, Combination therapy, and hyaluronic acid." The analysis reveals that Vesicles targeted drug delivery, cellular uptake, ultrasound, Chitosan, and Pegylation were identified as the research areas that require further attention in the field of liposomes as drug delivery research.

The findings of the research analyses of liposomes as drug delivery have been mapped in Figure 6.

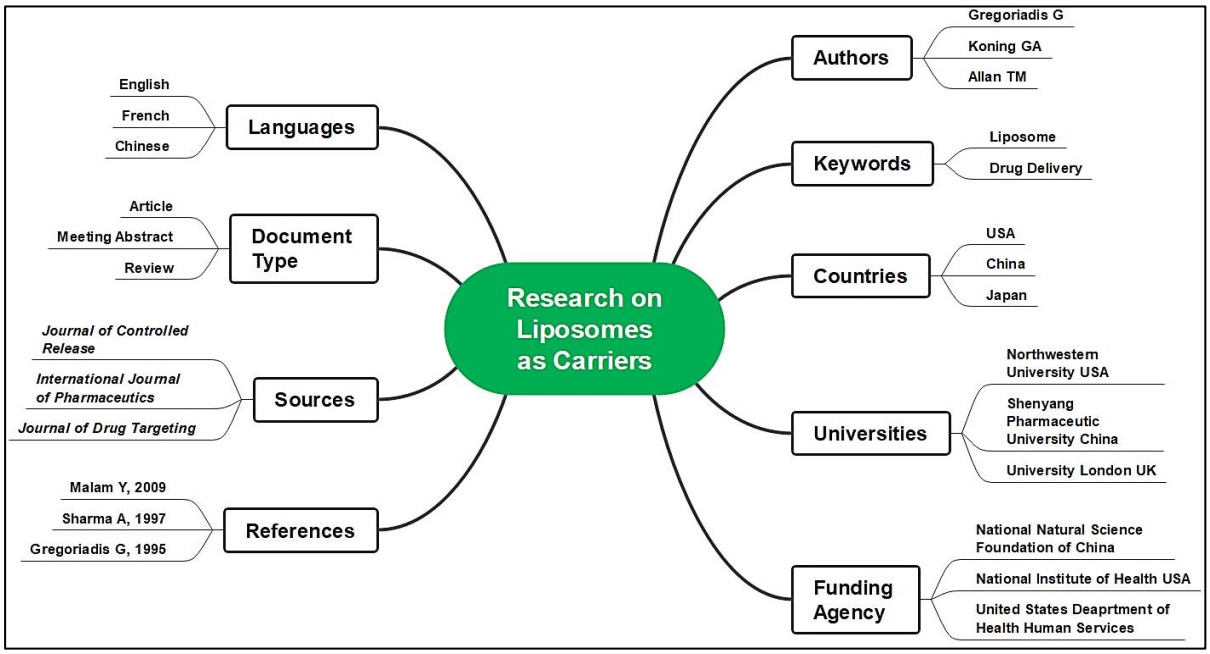


Figure 6: Mind Mapping of the Analysis

Discussion

This research aims to assess the literature on 'liposomes as drug delivery between 1980 and 2021. It has been observed that there are 629 research papers indexed in the Web of Science. Research productivity has increased exponentially in recent decades. The first research paper was recorded in 1980 with 351 citations. The literature produced an average of 5.72 papers yearly, with the most publications reaching 49 in 2018 and 2019. The highest number of total citations in 2004 was obtained for 34 publications in 2011. Hence, it indicated that publications, as well as citations on liposomes, are continuously growing. However, the average number of publications has not reached a high level, suggesting that this field still has much scope for

further detailed research and needs researchers' attention. As expected, most researchers preferred publishing in English, with 623 publications and 24740 citations. The analysis also indicated that researchers preferred to publish their studies as research articles (TP: 395). The Journal of Controlled release's most relevant source published the highest number of studies with 45 publications and 3063 citations, which first published the work on liposomes as drug delivery in 1990. Journal of Controlled Release publishes cutting-edge research in the delivery science and technology field. Sharma (2021) reported a similar result in his scientometric research on global liposome research during 2011-2020. The paper grabbed much attention across the globe and received the highest number of citations. The second most productive journal is the International Journal of Pharmaceutics, with 30 publications and 1587 citations. It publishes natural and clinical sciences articles and encourages submitting papers containing original research work. This result agrees with Robert et al. (2017), who examined research productivity of drug delivery based on the Web of Science between 1974 and 2015. The total number of authors is 2417, and they have appeared 3116 times. Thirty authors have single-authored documents to their account, while 2387 are authors of multi-authored. Analytically, there are 3.84 authors per document. Data analysis implies that there are 0.26 documents per author. It also implies that 4.95 co-authors per document suggest more collaborative work in this research area: a collaboration index of 4.02. Therefore, this indicated that the researcher preferred to collaborate in liposome research. Gregoriadis G is the fortunate 1st ranked author in terms of receiving more citations, winning 921 TC with seven publications, indicating the significance of his work in the field. Gregoriadis has made the first move towards using liposomes in drug delivery. His work in the field led to the clinical approval of liposome application (Gregory Gregoriadis & Perrie, 2010). The top ten listed cited papers ranged between 340 and 743 citations. The article entitled 'Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer' by Malam et al. (2009) was recognized as the most cited research paper on liposomes (743 citations), while the most cited reference noted as 'Recent advances with liposomes as pharmaceutical carriers'' by Torchilin (2005,) received the highest citations (53). Therefore, it is clear that research on liposome drug delivery impacts and gets attention from international researchers. It has been found that there are 1790 indexed keywords. The authors assigned 1332 keywords. However, the analysis was conducted to identify the research trend by considering the author keyword, such as "liposome," which is the frequently appearing keyword with 231 occurrences. This keyword analysis supports the results reported by Sharma (2021) and Zhou and Zhao (2015).The word "Drug Delivery" is next in line with 89 occurrences. The following author keywords are "doxorubicin," with 28 occurrences and 44 link strengths. The analysis unveils that publications on liposomes as drug delivery come mainly from the USA, with 181 records representing 28.77% of total documents. The same results were reported by (Zhou & Zhao, 2015) regarding the most productive county (USA) in Liposome research. China has been identified as the second leading contributor (104 records). China also placed 2nd most productive country, reported by Sharma (2021), followed by Japan (59 records), Italy (42 records), England (39 records), and the Netherlands (35 records). The analysis implies that most of the top research has been produced by developed countries compared to developing countries. The research also observed a similar pattern (Robert et al., 2017). Regarding international collaboration in producing liposome research, China emerged as a top collaborator with the USA (19 publications). Followed by the Netherlands with Germany (9 publications) and France (6 publications). Yet again, the most

productive institution is from the USA, China, and the UK. Shenyang Pharmaceutical University China, University of London UK, and Northwestern University USA have the highest records, i.e., 11 publications. "National Natural Science Foundation" from China-funded 64 research. It bagged first in the top 19 list, followed by "The National Institute of Health" from the USA and "The United States Department of Health Human Services," which produced 49 records. Most funding agencies are from the USA, China, and Japan. The thematic evolution of authors keyword revealed that permeability, ocular drug delivery, chemotherapy, cancer therapy, hypoxia, combination therapy, and hyaluronic acid were research topics that had gained recent popularity. However, vesicles, targeted drug delivery, cellular uptake, ultrasound, chitosan, and pegylation were identified as the research areas that require further attention in the field of liposomes as drug delivery research. The findings of the research analyses of liposomes as drug delivery have been mapped in figure 7.

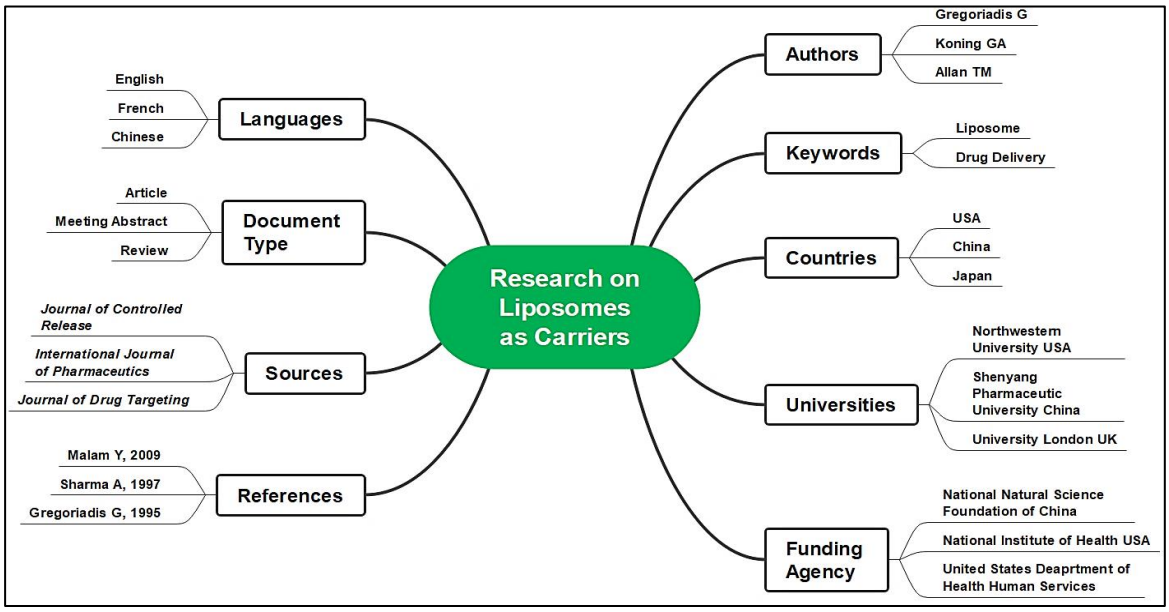


Figure 7: Mind Mapping of the Analysis

Conclusion

The advanced evaluative details supplied by bibliometric analysis include authors, institutions, research fields, nations, universities, and document formats. It will provide a data-driven overview of liposome research in the drug delivery domain and offer readers evidence-based descriptions, comparisons, and visualizations. It also will be helpful to understand the specific areas of research that the authors analyzed. This study clearly shows that there is a wide range of studies in areas such as "target delivery," "liposome stability," and "chemotherapeutics release," among others. Over time, there has been a gradual increase in liposome publications and their usage in drug administration. The United States, China, and the Netherlands are among the top ten countries contributing to the literature, with authors from France, Canada, and Japan collaborating. The top 10 journals with the highest publications focus on pharmaceuticals. The study makes two recommendations; the first is to expand the number of conferences, which will aid aspiring researchers interested in using liposomes as medication carriers to improve the chances of curing various disorders. Second, professional liposomes and

drug delivery publications should lead in attracting new research and publicizing its publication. Furthermore, the analyses indicate that the most active research areas are permeability, ocular drug delivery, chemotherapy, cancer therapy, hypoxia, combination therapy, and hyaluronic acid. However, the authors identified that areas such as vesicles, targeted drug delivery, cellular uptake, ultrasound, chitosan, and pegylation require more attention from the researchers in the field.

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