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Scientometric analysis of global publication output in liposome research (2011-2020)

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Abstract

The paper examines 32855 papers published on liposome research during the years 2011−20, as listed in the Scopus database. The global publication output on liposome research increased from 2907 in 2011 to 3695 in 2020 with average annual growth of 2.76%. The United States was the most productive country in liposome research followed by China and India. The maximum number of papers on liposome research were published by researchers from the Ministry of Education China (640 publications), CNRS (550 publications), and the Chinese Academy of Sciences (454 publications). Biochemistry, Genetics and Molecular Biology account for the largest number of publications in liposome research. Journal of Controlled Release published the maximum number of publications on liposome research during this period. Hideyoshi Harashima from Hokkaido University, Japan was a leading author in liposome research with the maximum number of publications.

Keywords: Liposome; scientometric analysis; nanoparticles; research productivity; research trend

1. Introduction

The liposomes are an important nano-sized drug delivery system with distinct properties, such as ease of preparation, characteristic bilayer structure, and excellent biocompatibility (Bozzuto & Molinari, 2015; Li et al., 2019). A substantial attempt has been done over the last several decades to develop liposome-based drug delivery systems. Several drugs have been encapsulated in liposomes to reduce toxicity and to extend the duration of the therapeutic effect (Alavi et al., 2017; Sharma et al., 2020). Various liposomal-based systems have been approved by the FDA and are undergoing clinical trials involving a broad range of anti-cancer, anti-viral, and anti-bacterial applications (Crommelin et al., 2020; L. Liu et al., 2019; Tahara et al., 2018). Further advances in the optimization of liposome-based drug delivery systems using various preparation techniques and an expanded application to new modalities such as nucleic acid therapy, immunotherapy, CRISPR/Cas9 therapeutic approaches have also been investigated to meet the continued demands for new drugs in the clinic (Gao et al., 2019; Zhen & Li, 2020). In recent years, several functionalities have also been introduced to liposomes, including in vivo imaging probes, temperature and ph-sensitive moieties, and novel agents for photothermal and photodynamic therapies (Belfiore et al., 2018; Lamichhane et al., 2018).

In recent years, scientometrics and bibliometrics have been widely applied in various fields to identify the productivity of authors, institutions, and countries, international collaborations, and to identify the

research trends in a specific subject area (Sharma, 2019; Sharma et al., 2019; M. H. Wang et al., 2011). Although the interest in liposome research has been increasing, very few studies were carried out from a global perspective for measuring and analyzing scientific publications on liposome research. Zhou et al. performed a bibliometric analysis of global liposome research during 1995–2014 using data retrieved from the Web of Science database (Zhou & Zhao, 2015). The present study aims to analyze the publication growth rate, most productive subject areas, recent research trends, leading countries, top funding agencies, top organizations, most prolific authors, and most productive journals publishing research in the subject based on the data exported from SCOPUS database. SCOPUS is regarded as one of the largest databases of peer-reviewed literature covering a broad variety of subjects (Boyle & Sherman, 2005).

2. Materials and methods

The publication data for the present study was exported from the SCOPUS database [https://www.SCOPUS.com]. A search was carried out in the SCOPUS database using the keyword ‘‘Liposome’’ and results were filtered by publication year from 2011 through 2020. The complete metadata was exported to MS-excel in CSV format containing the citations and bibliometric information. The publication data was imported to SciVal [https://www.Scival.com] for further analysis. Several publication-quality indicators were employed to help identify publications and citation trends such as citations per paper (CPP), field weighted citation impact (FWCI), international collaborative papers (ICP), and h-index (Avanesova & Shamliyan, 2018; Sharma, 2021). The CPP is calculated by dividing the total number of citations by the total number of publications. The FWCI compares the total citations received by publications of an entity with the global average for the similar subject field, publication type, and publication year. The global average of the FWCI is taken as 1. International collaborative papers (%) represent the percentage of papers published with international co-authors. h-index was regarded as the h of Np articles were cited no less than h times each and the other (Np-h) articles were cited no more than h times each (Hirsch, 2005). >100 indicates the number of papers with more than 100 citations and >50 indicates the number of papers with more than 50 citations.

3. Analysis and results

3.1 Characteristics of Publication Output

The year-wise distribution of publication output revealed the progress of research on liposomes over time (Table 1, Figure 1). Global research output in liposome research consisted of 32855 publications during 2011-20 and registered an average annual growth rate of 2.76%. The articles published during 2011-20 had an average citation per paper of 21.3 and international collaboration of 24%. The number of global scientific publications increased from 2907 in 2011 to 3695 in 2020. Of the total publications,

75.05% (24659) appeared as articles, 17% (5586) as reviews, 3.01 % (990) as a book chapter, and 2.31% (759) as conference papers. Other types of publications contributed less than 2.62% share.

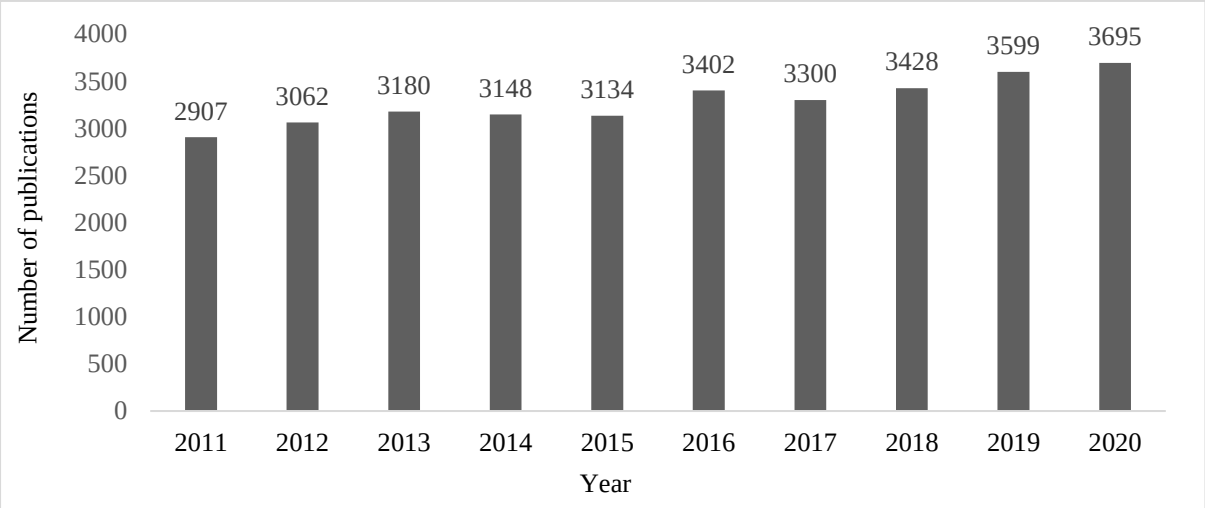

Figure 1. Global publication output in liposome research during 2011-20

Table 1. Global publication output during 2011-20

Year	TP	AGR (%)	TC	CPP	ICP (%)
2011	2907	-	107401	36.9	20.7
2012	3062	5.33	112319	36.7	21.6
2013	3180	3.85	103123	32.4	20.4
2014	3148	-1.01	92106	29.3	23.3
2015	3134	-0.44	78795	25.1	23.2
2016	3402	8.55	71717	21.1	24.7
2017	3300	-3	56473	17.1	24.3
2018	3428	3.88	42730	12.5	26
2019	3599	4.99	26959	7.5	26.7
2020	3695	2.67	7708	2.1	27.3
2011-2015	15431	-	493744	32.0	21.9
2016-2020	17424	-	205587	11.8	25.9
2011-2020	32855	-	699331	21.3	24

TP=Total publications; TC=Total citations; CPP=Citations per paper; ICP=International Collaborative Papers

The subject areas (as defined by the SCOPUS database) were used as criteria for understanding the distribution of liposome research during 2011-20. Biochemistry, Genetics and Molecular Biology accounted for the largest publications share (40.8%), followed by Pharmacology, Toxicology and

Pharmaceutics (35.93%), Medicine (23.28%), Chemistry (22.87%), and Materials Science (17.32%). Among these subject areas, Chemical Engineering registered the highest citation per paper of 25.5, followed by Engineering (25.4), and Materials Science (25%). Subject-wise distribution of global publication output in liposome research during 2011-20 is shown in Table 2.

Table 2. Subject-wise distribution of Indian publications in liposome research during 2011-20

S. No.	Subject	TP	% TP	TC	CPP
1	Biochemistry, Genetics and Molecular Biology	13391	40.76	288936	21.6
2	Pharmacology, Toxicology and Pharmaceutics	11806	35.93	283430	24.0
3	Medicine	7648	23.28	142336	18.6
4	Chemistry	7513	22.87	152498	20.3
5	Materials Science	5691	17.32	142102	25.0
6	Chemical Engineering	5343	16.26	136444	25.5
7	Engineering	4070	12.39	103251	25.4
8	Physics and Astronomy	3139	9.55	67180	21.4
9	Immunology and Microbiology	1939	5.90	41036	21.2
10	Agricultural and Biological Sciences	1487	4.53	26874	18.1

TP=Total publications; TC=Total citations; CPP=Citations per paper

3.2 Most productive countries

Publication data of the top 10 most productive countries in liposome research during 2011-20 is shown in Table 3 and Figure 2. The top 10 most productive countries contributed 85.66% share of global publication output. The United States tops the list with a global publication share of 21.6%. China ranks second (with a publication share of 19.41%), followed by India (8.05%), Japan (7.75%), Germany (6.23%). The United States had the highest h-index (178), followed by China (107), and Germany (92). The United Kingdom registered the highest citation per paper of 30.4 followed by Canada (28.6), and South Korea (27.1). The United Kingdom had the highest FWCI of 1.83. Researchers from the United Kingdom published the highest number of internationally collaborative papers (62.4%), followed by authors from Germany (60.7%) and France (57.6%). The United States produced the maximum number of highly cited papers with more than 100 and 50 citations. The proportion of self-citations was lowest in papers published by the United Kingdom (3.38%), while the proportion of self-citations was highest in papers published by China (10.4%).

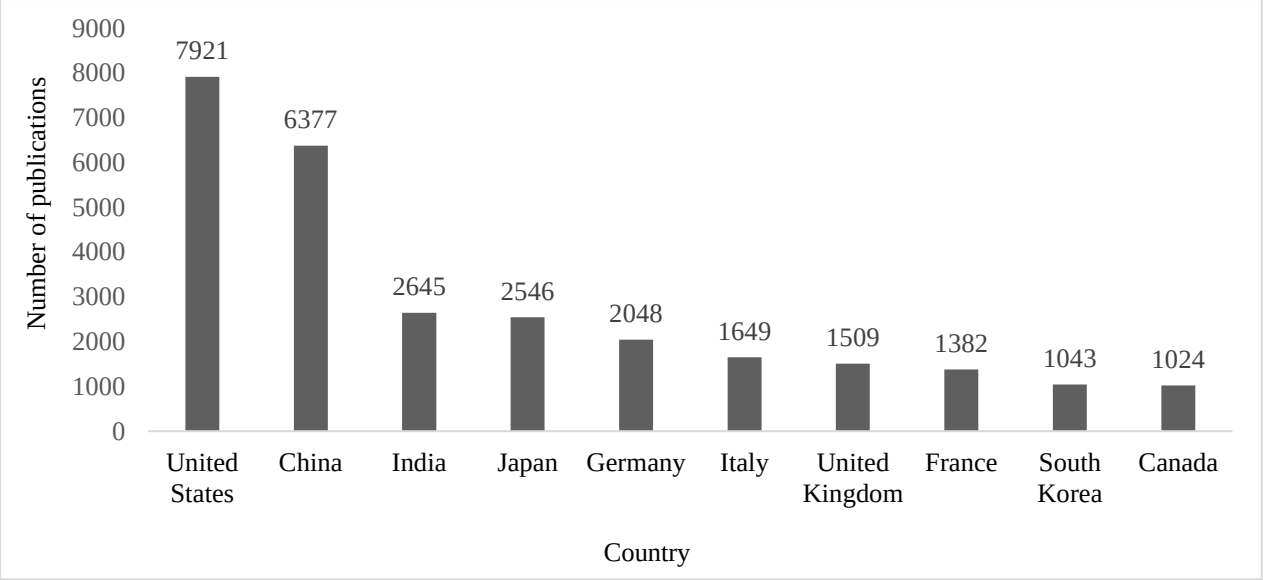

Figure 2. Top 10 most productive countries in liposome research during 2011-20

Table 3. Publication data of top 10 most productive countries in liposome research during 2011-20

Rank	Country	TP	TP (%)	TC	SC (%)	CPP	FWCI	ICP (%)	>100	>50	h-index
1	United States	7921	24.11	240708	6.94	30.4	1.79	39.6	426	1151	178
2	China	6377	19.41	108610	10.44	17	1.35	20.7	124	470	107
3	India	2645	8.05	45254	8.19	17.1	1.19	23.7	62	191	83
4	Japan	2546	7.75	44914	9.50	17.6	1.1	22.5	47	160	77
5	Germany	2048	6.23	51997	4.21	25.4	1.57	60.7	83	237	92
6	Italy	1649	5.02	38346	8.62	23.3	1.66	46.6	38	189	78
7	United Kingdom	1509	4.59	40798	3.38	27	1.83	62.4	74	204	87
8	France	1382	4.21	34070	4.38	24.7	1.59	57.6	52	174	79
9	South Korea	1043	3.17	28293	3.41	27.1	1.61	31.9	36	108	69
10	Canada	1024	3.12	29278	4.07	28.6	1.6	51.1	40	122	71

TP=Total publications; TC=Total citations; SC=Self citations; CPP=Citations per paper; FWCI= Field weighted citation impact, ICP=International Collaborative Papers; >100=Number of papers with more than 100 citations, >50= Number of papers with more than 50 citations

3.3 Journal Analysis

The top 10 journals publishing papers in the liposome research during 2011-20 are shown in Table 4. In the time frame analyzed, 40.33% of articles on liposome research were published as open access.

The top 10 most productive journals publishing articles in the field of liposome research during 2011-2020 together contributed 5079 papers to global publication output with a publication share of 15.46%. Journal of Controlled Release had the highest publication output (857), followed by the International Journal of Pharmaceutics (763) and International Journal of Nanomedicine (142). Among these most productive journals, Biomaterials registered the highest citation per paper of 55.5, followed by Journal of Controlled Release (48.2), and International Journal of Nanomedicine (30.4). Journal of Controlled Release had the highest h-index of 93, followed by Biomaterials (75), and International Journal of Pharmaceutics (61). Journal of Controlled Release received the highest FWCI of 3.61 and published the maximum number of highly cited papers with more than 100 and 50 citatio.

Table 4. Top 10 journals publishing papers in the liposome research during 2011-20

S. No.	Journal Name	TP	TC	CPP	FWCI	ICP (%)	>100	>50	h-index	CiteScore 2019
1	Journal of Controlled Release	857	41288	48.2	3.61	31.4	80	254	93	14.4
2	International Journal of Pharmaceutics	763	18258	23.9	2.61	26.9	16	89	61	7.6
3	International Journal of Nanomedicine	550	16715	30.4	1.51	21.3	25	69	57	7.1
4	Biochimica Et Biophysica Acta Biomembranes	519	9302	17.9	0.97	33.5	3	29	44	7.8
5	Colloids and Surfaces B Biointerfaces	499	9610	19.3	1.17	27.9	4	46	48	7.1
6	Langmuir	481	8161	17	1.08	32.2	3	33	44	6.1
7	Plos One	409	8008	19.6	0.95	30.4	2	27	42	5.2
8	Biomaterials	365	20242	55.5	2.85	29.3	43	145	75	18.7
9	Journal of Liposome Research	341	3833	11.2	1.2	17.6	0	8	27	4.1
10	Scientific Reports	295	4539	15.4	0.86	36.1	4	14	31	7.2

TP=Total publications; TC=Total Citations; CPP=Citations per paper; FWCI= Field weighted citation impact, ICP=International collaborative papers; >100=Number of papers with more than 100 citations, >50= Number of papers with more than 50 citations

3.4 Top 10 funding agencies

The top 10 funding agencies in liposome research are shown in Figure 3. National Natural Science Foundation of China funded 2367 publications during 2011-20 and stands first followed by National Institutes of Health (1863 publications), Department of Japan Society for the Promotion of Science

(1466 publications), National Cancer Institute (1092), and National Institute of General Medical Sciences (1030 publications). Table 4 shows the top ten funding agencies that are financially assisting research activities in the field of liposome research.

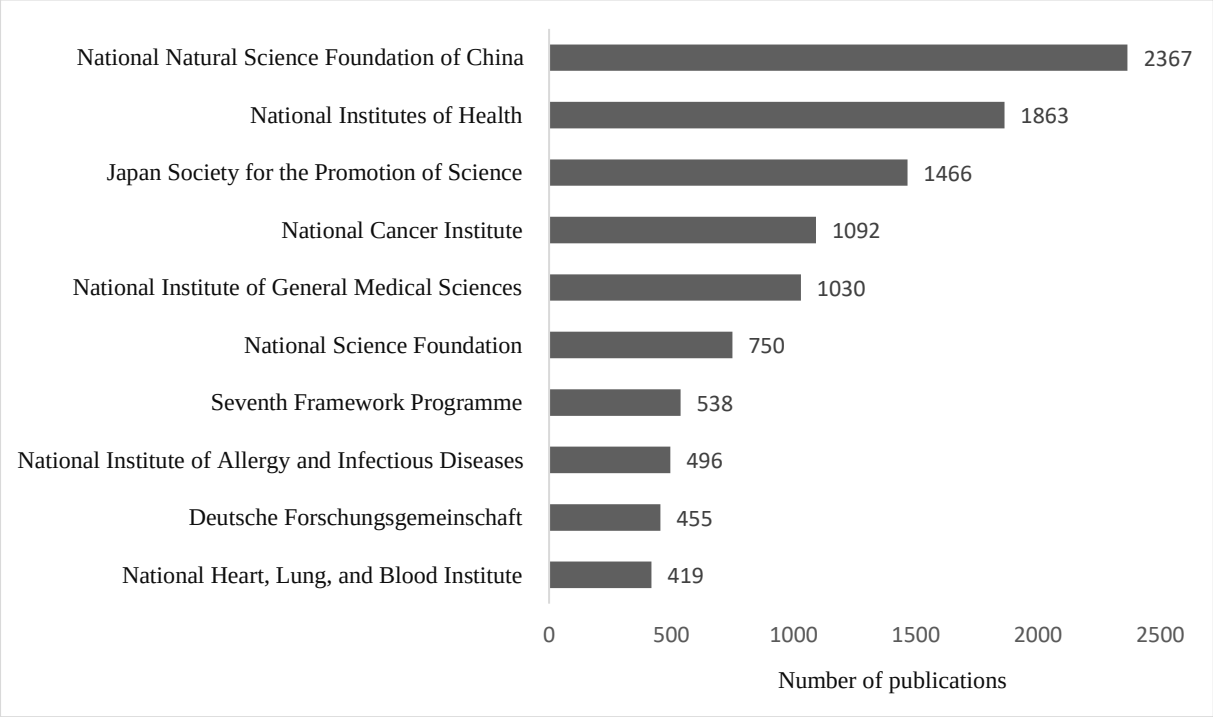

Figure 3. Top 10 funding agencies in liposome research

3.5 Contribution and impact of most productive organizations

The research performance of the top 15 most productive global organizations in the field of liposome research during 2011-20 is given in Table 5. These 15 organizations account for 14.49% (4761 publications) of total global publication output. Ministry of Education China (640 publications) was the most productive organization followed by CNRS (550 publications), and the Chinese Academy of Sciences (454 publications). Harvard University registered the highest citation per publication of 53.5, followed by Utrecht University (44), and the Chinese Academy of Sciences (31.2). The average citation per paper of these 15 organizations was 24.4. Chinese Academy of Sciences and CNRS registered the highest h-index (57 each). The University of Copenhagen published the highest number of papers with international collaboration (63.5%), followed by Utrecht University (62.4%), and Harvard University (55.6%). Utrecht University recorded the highest FWCI of 3.2. Chinese Academy of Sciences produced the highest number of highly cited papers with more than 100 and 50 citations.

Table 5. Top 15 Indian institutions in the field of clean water and sanitation research during 2011-20

S. No.	Organization Name	TP	TC	CPP	FWCI	ICP (%)	>100	>50	h-index
1	Ministry of Education China	640	10793	16.9	1.6	22	9	42	48
2	CNRS	550	12693	23.1	1.48	53.6	18	65	57
3	Chinese Academy of Sciences	454	14160	31.2	2.19	26.9	27	67	57
4	Sichuan University	359	7015	19.5	1.69	12.8	8	31	43
5	Harvard University	306	16356	53.5	3	55.6	20	45	48
6	Inserm	284	5920	20.8	1.49	44.4	7	29	39
7	National Research Council of Italy	282	6247	22.2	1.36	38.3	7	24	37
8	Universidade de Sao Paulo	278	4480	16.1	1.08	39.9	4	20	34
9	University of Copenhagen	255	6453	25.3	1.57	63.5	8	36	44
10	Shenyang Pharmaceutical University	236	4778	20.2	1.86	12.7	4	15	36
11	Utrecht University	234	10292	44	3.2	62.4	20	45	48
12	Peking University	225	6754	30	2.02	14.7	12	45	48
13	Osaka University	224	3199	14.3	0.98	16.5	2	16	30
14	China Pharmaceutical University	219	4504	20.6	1.79	23.7	7	16	34
15	Russian Academy of Sciences	215	1874	8.7	0.74	29.3	0	2	23

TP=Total publications; TC=Total citations; CPP=Citations per paper; FWCI= Field weighted citation impact, ICP=International Collaborative Papers; >100=Number of papers with more than 100 citations, >50= Number of papers with more than 50 citations

3.6 Most prolific authors

The Scientific productivity of the top authors on liposome research during 2011-20 is presented in Table 6. The 10 most productive authors together contributed 841 papers and generated 27652 citations during 2011-20. Of the top ten contributing authors, Hideyoshi Harashima was the most productive author with 133 publications. Gert A. Storm was in second place with 115 publications followed by Mahmoud Reza Jaafari with 112 publications. Vladimir P. Torchilin registered the highest citation per publication of 73.3 among these authors, followed by Qiang Zhang (49.3), and Gert A. Storm (46.9). Gert A. Storm received the highest h-index of 37, followed by Vladimir P. Torchilin (33), and Hideyoshi Harashima (32). Robert Jian Guang Lee published the highest number of internationally collaborative papers (83.8%). Vladimir P. Torchilin and Zhirong Zhang registered the highest FWCI of 2.98. Vladimir P. Torchilin published the maximum number of highly cited papers with more than 100 and 50 citations.

Table 6. Top 10 authors in the field of liposome research during 2011-20

S. No.	Author name	Current affiliation	TP	TC	CPP	FWCI	ICP (%)	>100	>50	h-index
1	Hideyoshi Harashima	Hokkaido University, Japan	133	3875	29.1	2.12	9.8	6	22	32
2	Gert A. Storm	Yong Loo Lin School of Medicine, Singapore	115	5394	46.9	2.72	60.9	9	23	37
3	Mahmoud Reza Jaafari	Mashhad University of Medical Sciences, Mashhad, Iran	112	1617	14.4	1.52	18.8	0	3	26
4	Vladimir P. Torchilin	Samarkand State Medical Institute, Uzbekistan	81	5938	73.3	2.98	34.6	15	25	33
5	Robert Jian Guang Lee	Jilin University, China	68	1586	23.3	1.55	83.8	1	8	23
6	Kazuo Maruyama	Teikyo University, Japan	68	1552	22.8	1.47	4.4	1	6	20
7	Zhirong Zhang	Sichuan University, China	68	2009	29.5	2.98	5.9	3	11	27
8	Anna Maria Fadda	University of Cagliari, Italy	67	2119	31.6	2.54	68.7	1	16	30
9	Thomas Lars Andresen	Technical University of Denmark	66	1583	24	1.65	24.2	4	8	21
10	Maria Manconi	University of Cagliari, Italy	63	1979	31.4	2.69	77.8	1	15	28
11	Ryo Suzuki	Teikyo University, Japan	62	981	15.8	1.28	9.7	0	3	19
12	Hiroshi Umakoshi	Osaka University, Japan	62	569	9.2	0.61	8.1	0	1	12

13	Costas N. Demetzos	National and Kapodistrian University of Athens, Greece	61	754	12.4	1.26	31.2	0	1	16
14	Qin He	Sichuan University, China	61	2023	33.2	2.82	3.3	3	12	28
15	Qiang Zhang	Peking University, China	61	3005	49.3	2.84	6.6	7	20	30

TP=Total publications; TC=Total Citations; CPP=Citations per paper; FWCI= Field weighted citation impact, ICP=International collaborative papers; >100=Number of papers with more than 100 citations, >50= Number of papers with more than 50 citations

3.7 Recent research trends in liposome research

SciVal analysis tool by Elsevier was used to identify the top keyphrases and most popular topics in liposome research. The period 2015–2020 was chosen to explore key areas that have been a major focus of researchers in recent years. Only original articles were included for the analysis. Keyphrases provide a reasonable description of a publication's theme and could reveal the profile of an author's research preferences (Rabby et al., 2018). Table 7 shows the top 20 most frequently occurring keyphrases used in publications related to liposome research during 2015-2020. Liposome, vesicle, drug delivery system, lipid bilayer, doxorubicin, lipid, bupivacaine, nanomedicine, phospholipid, nanocarrier, curcumin, phosphatidylcholine, gene transfer, small interfering RNA, membrane lipid, paclitaxel, targeted drug delivery, obstetric delivery, drug liberation, macrophage were the most frequently used keyphrases in liposome related research during 2015-2020. Word cloud of top keywords in liposome research during 2015-2020 is presented in Figure 4. The Keyphrases such as theranostic medicine, photosensitizing agent, obstetric cancer, photodynamic therapy, controlled drug release, bupivacaine, liposomal doxorubicin, docetaxel, hyaluronic acid, nanoparticle, nanocarrier, extracellular vesicle, targeted drug delivery, targeting, microna, folic acid, permeation, prodrug, drug liberation, are gaining more popularity in recent publications in terms of publication growth.

Table 7. Top 20 most frequently occurring keyphrases on liposome research during 2015-2020

S. No.	Keyphrase	S. No.	Keyphrase
1	Liposome	11	Curcumin
2	Vesicle	12	Phosphatidylcholine
3	Drug Delivery System	13	Gene Transfer
4	Lipid Bilayer	14	Small Interfering RNA
5	Doxorubicin	15	Membrane Lipid
6	Lipid	16	Paclitaxel

7	Bupivacaine	17	Targeted Drug Delivery
8	Nanomedicine	18	Obstetric Delivery
9	Phospholipid	19	Drug Liberation
10	Nanocarrier	20	Macrophage

Figure 4. Word cloud of top keyphrases in liposome research during 2015-2020; keyphrase color legend: green – growing, blue – declining (Data source: SciVal)

3.8 Highly cited articles

The top 10 highly-cited research articles on liposome research during 2011-20 are shown in Table 8. "The targeted delivery of multicomponent cargos to cancer cells by nanoporous particle-supported lipid bilayers" by Ashley C.E. et al. published in the year 2011 in the journal "Nature Materials" was the top-cited article with a citation count of 779. Three more articles published during 2011-20 have received more than 500 citations so far. These include the articles titled "Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores" (published in Nature), "Mixed Lineage Kinase Domain-like Protein MLKL Causes Necrotic Membrane Disruption upon Phosphorylation by RIP3" (published in Molecular Cell), and "Pore-forming activity and structural autoinhibition of the gasdermin family" (published in Nature). These 10 most cited papers were published in 8 journals including 2 papers each in Nature and Nature Materials and 1 paper each in ACS Nano, Cell Reports, Molecular Cell, Nature Nanotechnology, Proceedings of the National Academy of Sciences of the United States of America, and The Lancet.

Table 8. Highly cited research articles on liposome research during 2011-20

S. No.	Title	Authors	Year	Journal Name	Citations
1	The targeted delivery of multicomponent cargos to cancer cells by nanoporous particle-supported lipid bilayers	(Ashley et al., 2011)	2011	Nature Materials	779
2	Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores	(X. Liu et al., 2016)	2016	Nature	722
3	Mixed Lineage Kinase Domain-like Protein MLKL Causes Necrotic Membrane Disruption upon Phosphorylation by RIP3	(H. Wang et al., 2014)	2014	Molecular Cell	685
4	Pore-forming activity and structural autoinhibition of the gasdermin family	(Ding et al., 2016)	2016	Nature	585
5	Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): A global, randomised, open-label, phase 3 trial	(Wang-Gillam et al., 2016)	2016	The Lancet	458
6	MLKL Compromises Plasma Membrane Integrity by Binding to Phosphatidylinositol Phosphates	(Dondelinger et al., 2014)	2014	Cell Reports	385
7	Magneto-aerotactic bacteria deliver drug-containing nanoliposomes to tumour hypoxic regions	(Felfoul et al., 2016)	2016	Nature Nanotechnology	371
8	Interbilayer-crosslinked multilamellar vesicles as synthetic vaccines for potent humoral and cellular immune responses	(Moon et al., 2011)	2011	Nature Materials	369
9	Microtubule-associated protein 1 light chain 3 alpha (LC3)-associated phagocytosis is required for the efficient clearance of dead cells	(Martinez et al., 2011)	2011	Proceedings of the National Academy of Sciences of the United States of America	364

10	Matrix metalloprotease 2-responsive multifunctional liposomal nanocarrier for enhanced tumor targeting	(Zhu et al., 2012)	2012	ACS Nano	347

4. Conclusion

Due to their distinctive structural features, physiological characteristics, and biological properties, liposomes have gained significant attention among the scientific community. These drug delivery systems are promising platforms for targeting, drug delivery, imaging, diagnostics, and theranostics (Akbarzadeh et al., 2013; Xing et al., 2016). This work focuses on the scientometric analysis of liposome research literature from the year 2011 to 2020 with SCOPUS data source. The findings of the study show that research on liposomes is progressing in recent years. Researchers from the United States, China, and India Korea contributed the most to the publications. The USA and China were ranked first and second in terms of the quantity of publication outputs. The United States had the highest h-index, followed by China, and Germany. These influential countries foster international collaborations and published a large number of papers with an international co-authorship. China and India were the only developing countries among the top 10 most productive countries. Journal of Controlled Release published the highest number of papers on liposome research followed by the International Journal of Pharmaceutics and International Journal of Nanomedicine. The use of liposomes in drug delivery has already had a significant effect in a variety of biomedical fields. The FDA has approved over a dozen liposome-based drug delivery systems, and several more are in various stages of development. Because of their biocompatibility and biodegradability, liposomes are attracting a growing number of new applications in the pharmaceutical and food industries. Liposomes are used in a variety of applications, including diagnostics, drug and gene delivery, cosmetics, and food nanotechnology. Future research will be able to improve on existing platforms and overcome current translational and regulatory limitations by better understanding the difficulties and developments in liposomal technology. When compared to an approved counterpart or current therapies, the cost-benefit analysis can be a stumbling block to the clinical translation of certain liposomal-based therapies. A better understanding of lipid interactions, rapid formulation screening, and the use of techniques to maximize clinical compatibility would help liposomes perform better in future diagnostic and therapeutic applications.

Conflict of interest

The author declare no conflict of interest.

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