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GLOBAL RESEARCH TRENDS REGARDING THE APPLICATIONS OF DENDRIMERS IN THE FIELD OF DENTISTRY - A BIBLIOMETRIC ANALYSIS

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Abstract

Objective- This bibliometric analysis aims to investigate the use of dendrimers in dental research trends. It is envisaged that this meticulous bibliometric analysis will shed light on the current state of the field and assist in eliminating barriers between research teams exploring into the clinical potential of dendrimers in dentistry around the world.

Methodology- We meticulously searched the Scopus database for articles on dendrimers. In order to extract bibliographic data, including details on study features and citation characteristics, the keyword "dendrimers" and its use in dentistry was employed. Based on the reference, the final included articles were ordered. The data was analysed and visualised using Ms Excel and the Vos programme. To assess the multiple connections between nations, organisations, authors, and publications, networking graphs were developed.

Result- In the initial search, 916 publications were discovered, and 53 articles were chosen based on inclusion criteria. The findings showed an upward trend in dendrimer research beginning in 2004, with the State Key Laboratory China—Li J and Liang K—and its organisations dominating the productivity. The leading donors were academics from China, Finland, and the United States of America.

Conclusion- The bibliometric study provides insightful data on current research trends with regard to the overall volume of publications on Dendrimers. Additionally, it provides a comprehensive study of researchers in this area and includes the leading countries and institutes conducting dendrimer research.

Clinical significance: The research on the effects of Dendrimer use in dentistry is summarised in this article. Dendrimers are gaining popularity worldwide, and scientific research into how to use them in dentistry has been progressing steadily.

Keywords- Dendrimers, Applications, Dentistry

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INTRODUCTION

A dendrimer is a macromolecule exhibiting a highly branching, three-dimensional structure, surface functionality, and flexibility. The main component of its structure is a multifunctional core molecule, which is surrounded by branches and end groups. The "Polymers of the Twenty-first Century" have been dubbed dendrimers. In 1978, dendrimer chemistry was initially introduced by Fritz Vogtle and colleagues[1]. He invented "cascade molecules" first. In 1985, Donald A. Tomalia developed the first dendrimer family[2]. TThe Greek words dendron, which means "tree," and meros, which means "part," are the roots of the word "dendrimer." Similar macromolecules were synthesised simultaneously, according to Newkome et al. in their first publication. They referred to them as "arborols," a word derived from the Latin "arbour," which also denotes a tree. Three main architectural elements are present in dendrimers: With the initiator acting as the core, the inner layer creates generations that are composed of external functional units and repeating units..[3,4]

Dendrimers are used in a wide range of domains, including the transdermal, oral, ophthalmic, pulmonary, and target-specific administration of drugs, microvascular extravasation, and the transfer of genes[5,6]. The size and form of hydroxyapatite can be altered by dendrimers using a variety of peripheral group modifications, generations, and dendrimer concentrations. Dendrimers are used in dentistry for a variety of purposes, including tooth remineralization, periodontal disease prevention, altering the surface of dental implants to enhance osseointegration, and enhancing the qualities of various dental biomaterials.[7] Dendrimers' unique chemical structure triggered a wave of scientific interest.[7,8]

Numerous dental disciplines, including general dentistry, use bibliometrics analysis. Bibliometrics provides a detailed account of data analysis that has been published in books, journals, and book chapters[9]. A bibliometrics is a quantitative technique for assessing the volume of scholarly literature that looks at several characteristics of research publications, such as citations, publications, institutions participating in the research, and geographical locations. [9] The use of bibliometric indicators facilitates measurement, evaluation, and comparison of the research output and impact of particular people and organisations.

In order to evaluate the progress of the research into dendrimers in dentistry, a bibliometric technique was used in this study. The goal is to examine research findings, publication and citation trends, top nations and universities, most productive authors, and top journals in the subject of dendrimers. Other objectives include identifying significant topics, keyword co-occurrences, and coupling regions, authors, and journals in the bibliography from 2004 to 2021. This thorough bibliometric analysis is anticipated to provide a clear picture of the current state of the field and assist in removing barriers between research groups studying the clinical potential of dendrimers in dentistry around the world.

Materials and methods

Data source

On July 17, 2022, the Scopus database's Science Citation Index Expanded (SCI-E) section was extensively searched. Dendrimers AND its use in dentistry were the search phrases. Title and abstract were independently scanned for each article that was identified through the search. There were no restrictions on language, publication date, Accepted Article status, or anything else. After a thorough title and abstract search, a second researcher

reviewed it. Any ambiguities in the abstract are sought by via a thorough text search. The inclusion requirements must be met by articles that discuss the use of dendrimers in dentistry. Applying dendrimers outside of dentistry is a requirement for exclusion.

Data extraction

The information was obtained, exported to Microsoft Excel, and organised by the quantity of citations. The papers were used to determine the features of the studies and the citations. Using MS Excel and the VOS viewer programme, the authors, nations, and keywords were analyse and the network visualised.

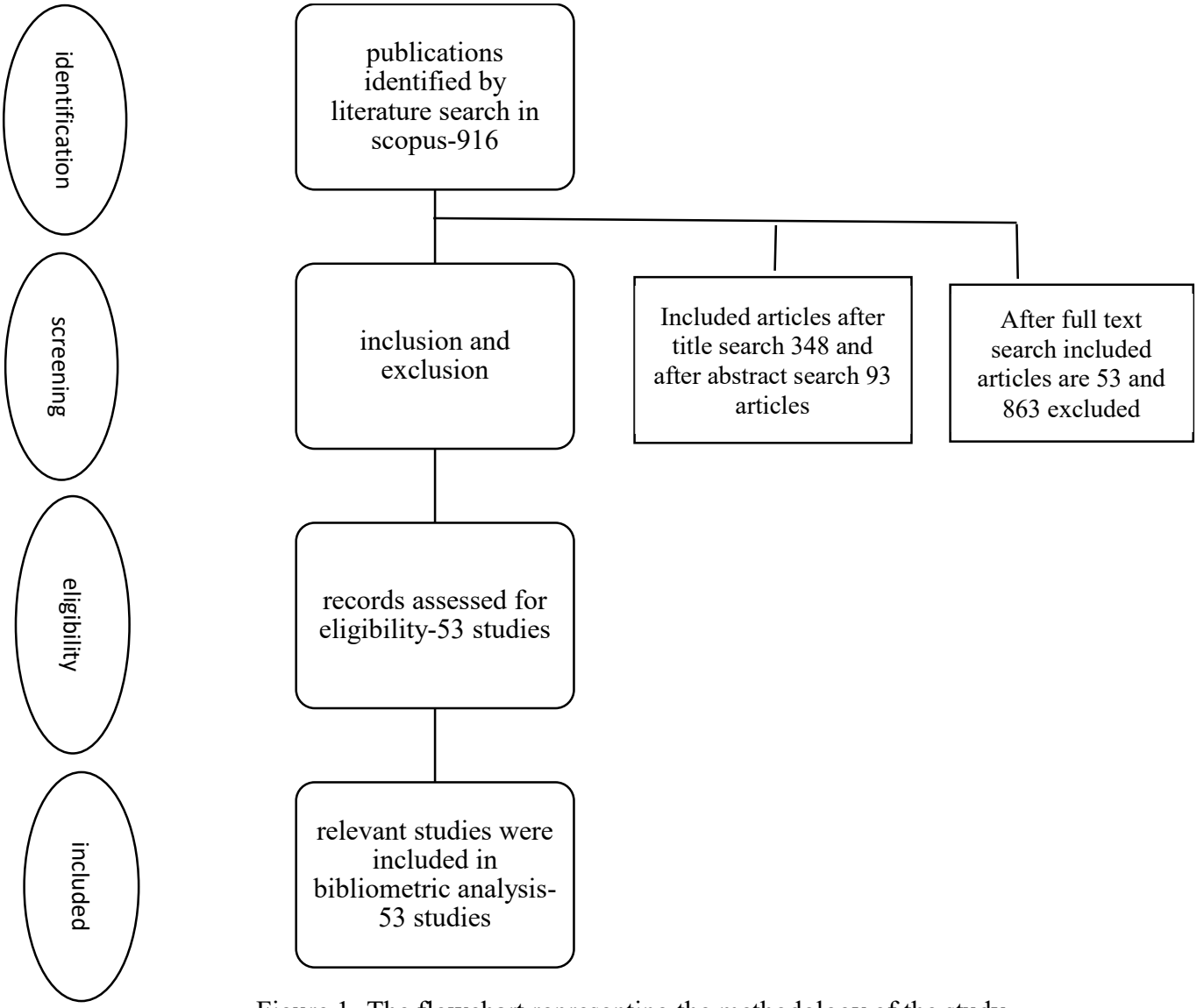

Figure 1- The flowchart representing the methodology of the study

Result:

A thorough search of 916 articles yielded a total of 53 items that were taken into account. The International Journal of Oral Science had the greatest impact factor of 24.8 among these 53 papers, and Li J. conducted the most research. The majority of the articles were published in 2004.

1.Year:

The dentistry article that was published had 26 citations in Scopus was from the year 2004. Following that, the volume of research production progressively increased over the course of the following year, with three papers earning an average of 36 citations. After 2005, there is a decline in research conducted in this area, with only one study completed at the conclusion of that decade.

There was a great deal of activity in the second decade of our century. Between the years of the current century, 37 publications were issued (2011–2020). Additionally, within this time period, the 2013 publications with the most citations (116) were published. The years 2021–2022, with around 11 articles, saw the highest number of publications, demonstrating a continuing growth in this field of study.

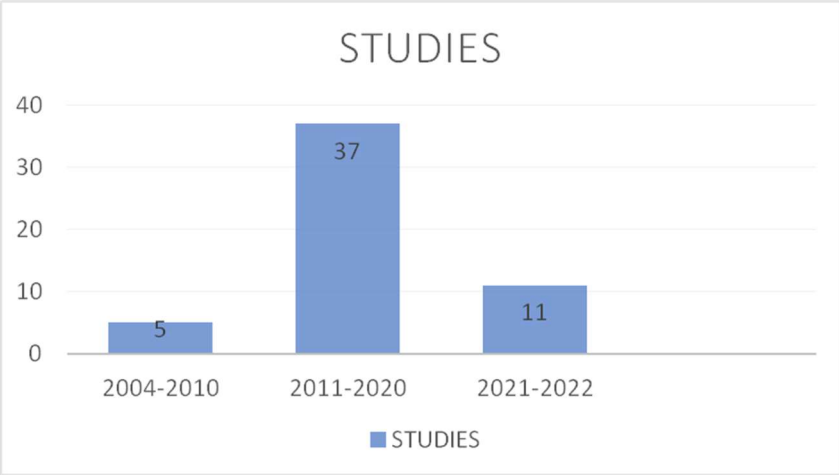

Figure 2- No of studies published pertaining to that year

Table 1- No of studies published in a year and the top cited article in that year

YEAR	No.of articles	Top cited in that year
2004	1	26
2005	3	36
2010	1	27
2011	3	36
2012	1	22
2013	1	117
2014	4	90
2015	5	37
2016	3	51
2017	7	25
2018	4	20
2019	5	21

2020	**4**	**10**
2021	**11**	**3**

2.Type of study

Among the 53 articles depending on the type of study most of the studies were invitro type-43 studies. Ex-vivo type of study were also done in 4 studies followed by 6 review articles

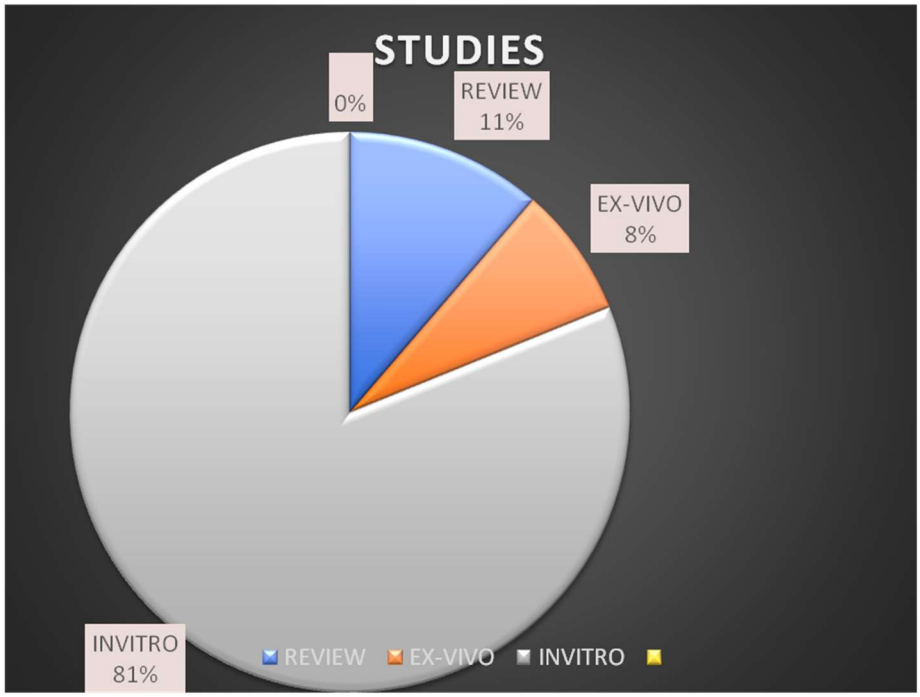

Figure 3- Type of studies – Denotes that major of the studies were invitro

Table 2- No. of studies done in each category

Invitro	Ex-vivo	review
5	**4**	**5**

3.Type of material:

Among the 53 articles that were based on the study's materials, 35 articles used PAMAM in their research without mentioning the generation, while 3 studies used carboxy terminated poly(amide-amine) and 4 articles used phosphate terminated PAMAM. Gen 4, Gen 3, Chlorhexidine-loaded poly(amide-amine), amine-terminated PAMAM dendrimers, and RGD-dendrimer conjugates were only a few of the many different types of PAMAM materials used in this study.

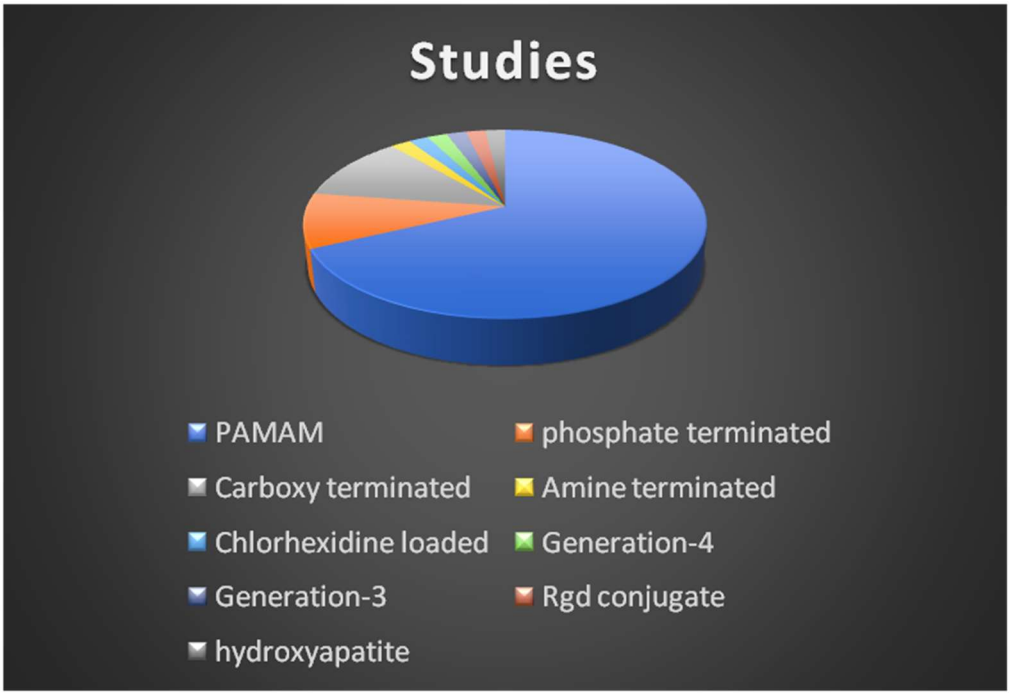

Figure 4- Type of materials used in the studies – Denotes that major of the studies used PAMAM

Table 3 – It denotes number of time each type of material used

Type of Material	No. of studies
PAMAM	**36**
Phosphate terminated	**5**
Carboxy terminated	**6**
Amine terminated	**1**
Chlorhexidine loaded	**1**
Generation-4 PAMAM	**1**
Generation-3 PAMAM	**1**
Rgd conjugate	**1**
Hydroxyapatite	**1**

4. Country:

Many of the 53 publications that are included in this list of studies were conducted in China, where nearly 35 research were conducted. Finland came next with 6 studies, then India 2, the United States 3, and Germany had each conducted 2 studies. Research in this field has only recently begun in certain nations, with one study each from Israel, Malaysia, Australia, Poland, and Mexico.

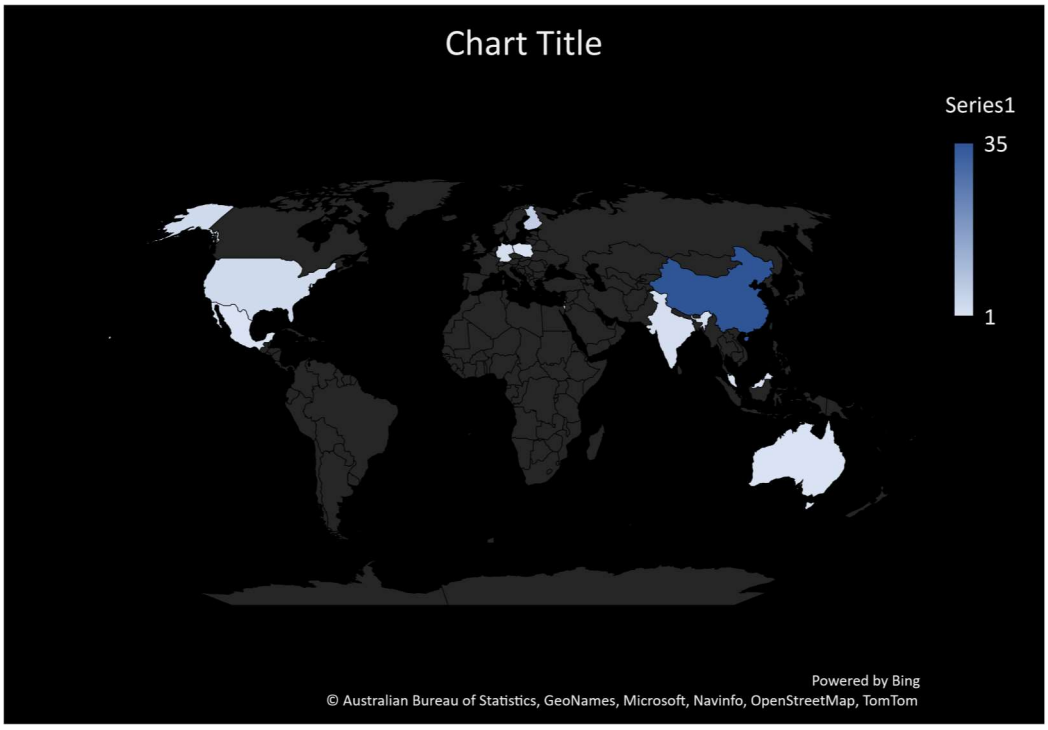

Figure 5- Countries involved in research of this material – Denotes the darker shade has done many studies compared to lighter shade and black countries are not involved in the study

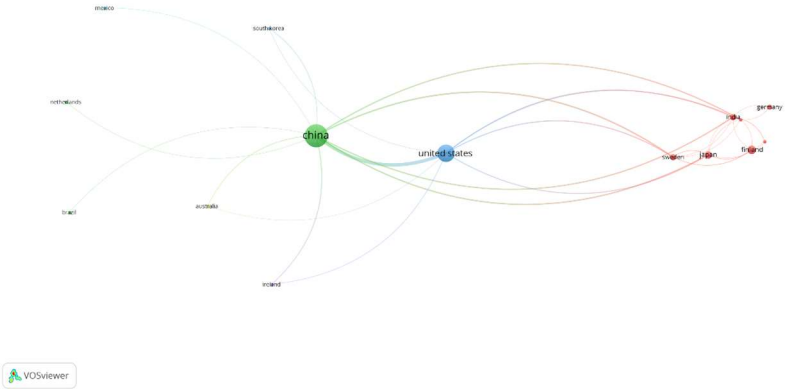

Figure 6- Countries involved in research of dendrimers. Image obtained by VOS software

5. Key words (Index Keywords-Co-Occurrence)

Dendrimer, biomimetics, biomimetic remineralization, and PAMAM are the most frequently used search terms in practically all papers. based on the image that VOS software produced.

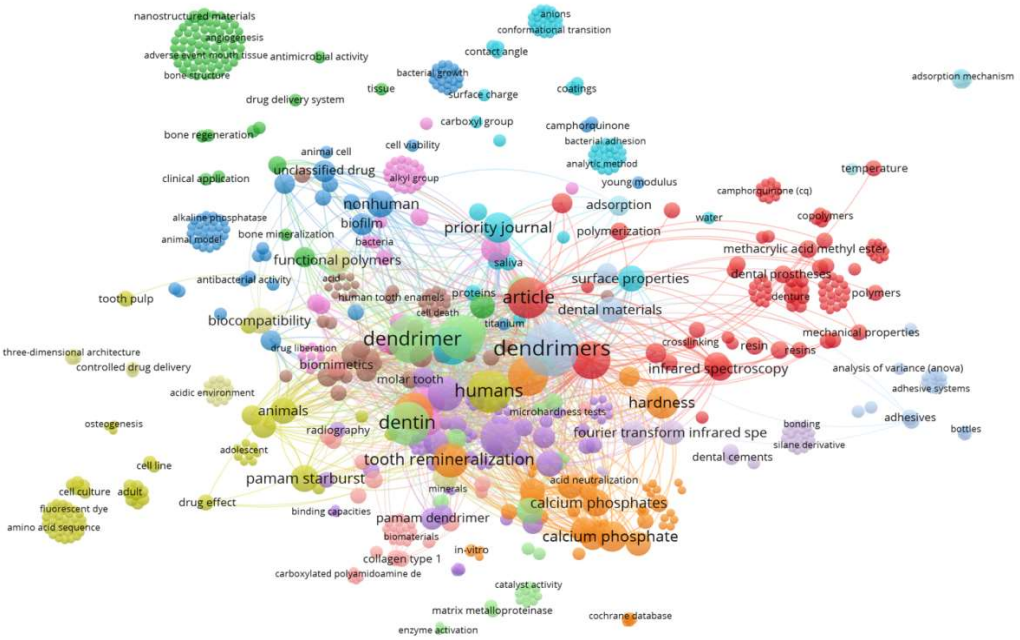

Figure 7- Keywords and its Co-Occurrence – bigger circle resembles highest occurrence and based on the link linkage of the words are analysed

Table 4-The number of times each keyword has occurred in the articles (only the top occurred keyword are specified based on VOS generated networking image)

RANK	KEYWORD	OCCURANCE
1	Dendrimers	35
2	Dendrimer	27
3	Humans	25
4	Dentin	23
5	Human	22
6	Article	20
7	Polyamidoamine dendrimer-PAMAM	19
8	SEM	19
9	Chemistry	17
10	Dental procedures	17
11	Tooth remineralization	14
12	remineralization	14
13	Hardness	12
14	Priority journal	11
15	Controlled study	10

6.H index:

Based on the authors of the study, the H index was examined for 53 articles. Scopus and Google Scholar have referred to H index numbers. For Li J. and Liang. K., the correspondence author who published the research, the highest h index was 85.

7.Impact factor:

On the basis of the journal's published papers, 53 articles' impact factors had been examined. Out of these 53 referenced papers, International Journal of Oral Science had the greatest impact factor (24.897).

8.Citation-Author

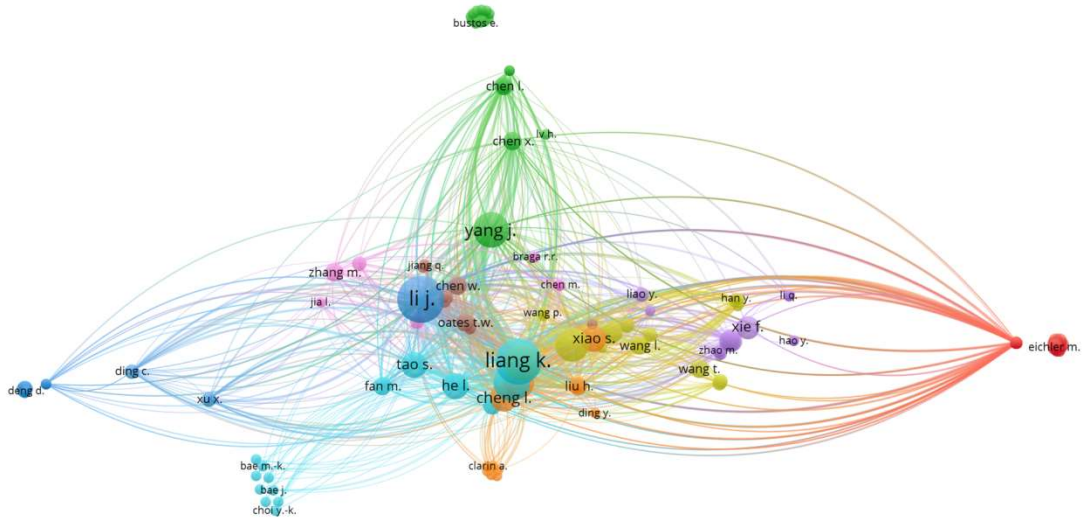

Figure 8- Denotes the analyses between the author and their citations and inter-relation swith other authors – Bigger circles denotes that the corresponding author has contributed to an greater extent

Based on the above image obtained by VOS software the highest number of studies were done by Li J (20 studies with 142 links) FOLLOWED BY Liang K (19 studies with 115 links) Yang J (11 studies with 129 links).

9.Citation of organization

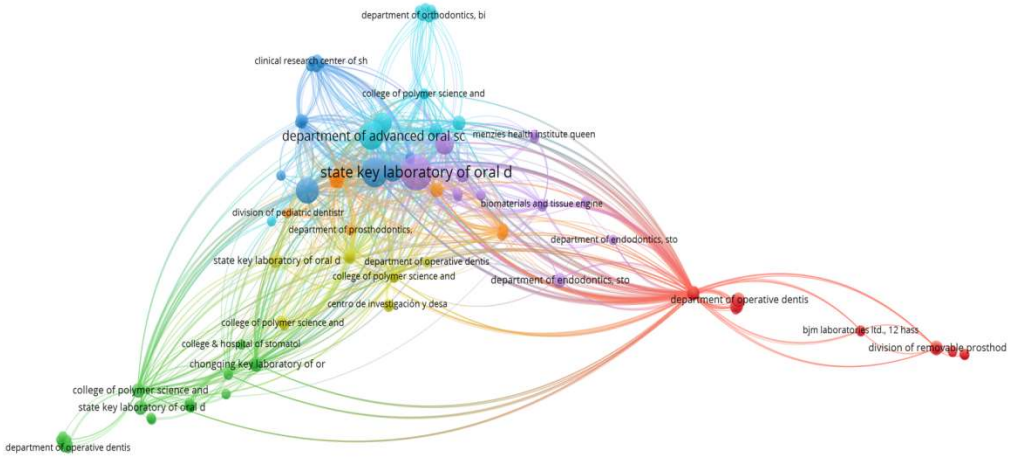

Figure 9 – Denotes that contribution of particular organisations towards the study and inter-relationship between the organizations

The Department of Advanced Oral Science and Therapeutics at the University of Maryland School of Dentistry came in second with 6 clusters and a total of 183 links and 7 publications, according to the mapping done in the VOS software, with almost 26 studies out of the 53 scientific studies done that were divided up based on the department and cited in the article.

Discussion:

As previously established, a dendrimer is a macromolecule that stands out for having a highly branched, three-dimensional structure that gives a high level of surface functionality and adaptability. (9)[8] High branching, multivalency, diverse chemical composition, well-defined globular formations, outstanding structural uniformity, and compatibility are some of the key characteristics of dendrimers. They are particularly well suited for biomedical applications like drug delivery, imaging, and tissue engineering. [1] The purpose of this study is to educate researchers on dendrimer uses in dentistry. Since dendrimers are a novel substance that can remineralize the tooth, its use has increased recently.

This is the first bibliometric study using an evidence-based methodology to examine dendrimers used in dentistry. The quantitative and qualitative technique of bibliometric analysis helps to understand how materials are used in dentistry [10].

Since Scopus is the largest database for abstract and citation search engines for peer-reviewed literature, it was used as a reference for this literature study. Scopus has more references that have been cited than Web of Science. It is used in several bibliometric research to assess publications as well as scientific data for analysis.[11]

Due to their evolving properties due to their new structures and specialised properties drawing increased attention, dendrimers are employed in dentistry for a variety of functions. The dendrimer's properties and uses can alter as a result of the functional groups it contains12. They are used as a remineralization agent, in composite and adhesive materials, in periodontology, and in implantology, among many other diverse applications in dentistry.[12]

Despite the fact that dendrimers were initially created in 1985, the first clear publications in the field of dentistry to appear in Scopus were made in China and the US in 2004. Due to the search being restricted to Scopus or the lack of significant developments in the field of dentistry, there was almost a five-year gap between 2005 and 2010. The number of studies has gradually increased between 2011 and 2020, peaking in 2017 with seven studies published, six of which were conducted in China and one in Mexico. Since the beginning, the most investigations have been conducted in 2021—10 studies total—with the first Indian study being published in this year. The article with the most citations in 2013 was published by China's State Key Laboratory of Oral Diseases, receiving 117 citations.

There have been numerous studies in this area up to this point, but the majority of them have been in vitro, and the few ex vivo studies that have been done have primarily used rats and hamsters. Some writers have conducted reviews focused on dendrimer applications specific to one field, such as dendrimer applications in orthodontics[13], etc.

A- The first Ex-vivo investigation was conducted in 2014 by Chen M. and Yang J. in a Chinese state laboratory using rats and extracted human teeth [14]

B- In their initial review papers, Noriega-Luna B. indicated the uses of dendrimers in drug delivery agents in 2014. [15]

Dendrimers are made in a variety of ways[16], and depending on their bonds and molecular structure, they can be classified into a large number of groups and subgroups. In general, the primary materials used are

PAMAM was first used as adhesive agent in 2004.[17] Phosphate Terminated-Phosphate-terminated PAMAM (PAMAM-PO3H2) -great dentin remineralization[18]Carboxy terminated-carboxylic-terminated PAMAM (PAMAM-COOH) regenerated intrafibrillar mineral[19]Amine terminated PAMAM (PAMAM-NH2) effective at regenerating minerals on the surfaces of dentine.[20]Chlorhexidine loaded-CHX and PAMAM-COOH were prepared similar way.[21] CHX-loaded PAMAM-COOH inhibit MMPs and induce in situ remineralization in the etched dentin[22]Generation-4 PAMAM are highly-branched polymers and have a large number of reactive end groups. [20]Generation-3 PAMAM, a sphere macromolecule with more functional ending groups supplies more nucleation locations to absorb Ca and P ions during remineralization.[23]Rgd conjugate –generation 5 (G5) dendrimers composed of arginine-glycine-aspartic acid (RGD), would modulate differentiation in dental pulp cells [24]

China is leading among the nations due to its large research output in this area, including studies that are not specifically related to dentistry. Finland ranks second, however there is a research time lag as Finland's most recent publication was published in 2011. US came in second with three studies, then came Germany and India. India has only recently begun research in this area, with the first publication being a review study and the second piece being an invitro study in 2021.

Each node in the network represents a specific entity (such as an article, author, country, institution, keyword, or journal) with the following characteristics:

A. The size of node denotes frequency of the keyword;

B. The link between nodes denotes co-occurrence of keywords.

C. The number of times that two keywords occur together or co-occur together is indicated by the thickness of the link between nodes in.

D. The bigger the node, the more frequent the keyword occurs, and the thicker the link between nodes, the more frequently the co-occurrences between keywords occur. The nodes and linkages in each hue correspond to a certain topic cluster.[25]

There were multiple keywords used in the study, however dendrimer, dendrimers, human, human, PAMAM, Dentin, SEM, article, etc. were the most often used ones. Each term is connected to additional words that are relevant to that specific study. Based on the type of material utilised, the study methodology, and the tests conducted, each study typically contains 3-5 keywords. There are numerous clusters visible in the image's corners, and they have an occurrence rate of 1-2 and are unrelated to any previous studies.

The amount of papers with citations makes up the H index. It is helpful in describing a researcher's scientific output[26]. The H index contrasts publications with citations to gauge quantity and quality. It is a method for determining the overall importance of a writer's scholastic production. The H index explains why some articles receive disproportionately more weight than others that aren't included. The 53 articles in the H index were examined using Google Scholar and Scopus. The highest H index score for the articles is 85.

A common technique to assess a journal's standing in comparison to other journals in the same area is to look at how many times its "average article" has been cited during a specific time period. While the "Impact factor" only applies to journals, the "H-index" applies to all publications. The study's highest impact factor was 24.897.[27]

Citation analysis, which functions under the assumption that citations imply intellectual linkages, is a crucial technique for scientific mapping. Through analysis, the most important papers in a field of study can be found. [28] Citations for authors aid in analysing the volume of work published in a field by a particular author and his

relationships with other co-authors. Li J. had the most publications with 19 but only two clusters, while Liang K. had 19 and was part in five cluster groups. Zhou[21] and Yang J[14], who have 12 and 11 publications, respectively, but participate in more than 5 cluster groups, are the next two.

The creation of dendrimers and their properties has attracted significant interest from a number of governments. China has demonstrated the most interest in dendrimers among the top emerging nations, both in terms of investment and curiosity. Highest number of studies conducted in China were from State Key Laboratory of Oral Diseases[29] Sichuan University, out of 35 studies, China has conducted around 26 of them. Dendrimer research has received limited attention from other developing countries, with an average of less than 5 publications. Due to its intriguing characteristics, we might anticipate further research from them in the upcoming years.

Limitations and Ideas for Future Research. This analysis was constrained by the use of a single database for the collection of bibliographic data. Other databases like Web of Science, PubMed, or Google Scholar were not taken into account. Despite its shortcomings, this study on dendrimers may aid future researchers by identifying possible research topics and filling in any gaps in the literature. Additionally, it would help them in their research as they looked for new partners and learned about the most prominent countries, universities, authors, publications, and keywords.

Future research could entail expanding the search to other databases and examining dendrimers' applications in medical research, such as cancer [30], drug delivery[16], and biological applications, in addition to those that are exclusive to dentistry. [31]

Conclusion

This bibliometric analysis provides detailed trends on a number of dendrimer-related topics from the publication of the first research article in 2004 through the most current time in 2021. It mostly gives us a sense of the amount of papers on dendrimers and the number of citations for those studies. Articles on this topic have generally been trending upward, with the number of publications notably rising after 2010 and reaching a peak between 2017 and 2021. The leading nations and organisations conducting dendrimer research as well as associated research trends have also been highlighted. Since dendrimers have so many different uses in dentistry, there was a noticeable surge in scientific publications last year, especially in light of how frequently they have been used lately. In order to comprehend the current state of the subject and identify any research lacunae that need to be filled, a detailed systematic study is necessary. However, Bibliometrics examines a wide range of attributes in research papers and aids in the assessment of the academic literature. Young and seasoned researchers alike should be able to imagine and establish future opportunities for potential scientific collaboration for use in research relevant to this sector thanks to the results of this study. The goal of this extensive bibliometric analysis is to give researchers with a thorough understanding of the current status of dendrimer research and to assist in bridging gaps amongst research clusters exploring the clinical application of dendrimers in dentistry across the globe.

Declarations of Competing Interest

The authors declare no conflict of interest.

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Authors' Contribution

1. Sri Meghana: Contributed to conception, design, data acquisition, analysis and interpretation, drafted and critically revised the manuscript

2. Sujitha ponraj: Contributed to conception, design, data acquisition, analysis and interpretation, drafted and critically revised the manuscript

3. Kavitha R: Contributed to conception, design, data acquisition and interpretation, drafted and critically revised the manuscript

4. Victor Samuel A: Contributed to conception, design, data acquisition, interpretation, critically revised the manuscript

5. Raja Kumar: Contributed to conception, design, data acquisition, interpretation, critically revised the manuscript

All authors gave their final approval and agree to be accountable for all aspects of the work

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