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Original Article

Evaluating Global Research on Photodynamic Therapy in Skin Cancer through Bibliometric Analysis

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Abstract

Photodynamic therapy (PDT) is a potential non-invasive therapeutic option for several cancer types, including skin cancer. Because PDT uses a focused and localized approach to treatment, there has been an increase in interest in researching its use in the management of skin cancer in recent years. In this work, we performed a bibliometric analysis to assess the body of knowledge and developments around PDT in skin cancer. Using information from the Web of Science database, this study used bibliometric research techniques to examine how the field of PDT for skin cancer is developing. To gather pertinent research publications published between January 1991 and July 23, 2023, a methodical search query was developed. Based on the 1654 records that were found, the analysis examined factors including the growth, influence, contributions, top authors, publications, institutions, keywords, research topics, and networks of collaboration between authors, sources, nations, and significant funding organizations. The results showed a steady growth rate of 4.44% for publications. The most productive organization was the University of Sao Paulo, which is in Brazil, and the most prolific author was researcher Haedersdal M. The British Journal of Dermatology, which is published by Wiley in the UK, is very influential in the area as evidenced by its top citation ranking. The study topics were mostly actinic keratosis, basal cell carcinoma, photodynamic treatment, and skin cancer. Notably, the National Cancer Institute of the US NIH was a major backer of scientific study in this field. For academics, physicians, and policymakers engaged in developing and applying PDT for skin cancer therapy, the findings of this study will add to the body of current information and support the use of evidence-based decision-making.

Keywords:

Photodynamic therapy
Photosensitizers
Skin cancer

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1. INTRODUCTION

Photodynamic therapy (PDT) has emerged as a viable therapeutic option for skin cancer, with benefits over traditional techniques such as radiation and chemotherapy. PDT employs light-activated photosensitizers (PSs), which create reactive oxygen species (ROS) and kill cancer cells. PDT has shown promising results in the treatment of many forms of skin cancer, including basal cell carcinoma, squamous cell carcinoma, and actinic keratosis. Clinical investigations have found that PDT patients had reasonable total response rates and favorable aesthetic outcomes. Furthermore, PDT successfully treats superficial skin lesions and early-stage skin malignancies, making it a viable option for minimally invasive therapies. PDT is a novel and successful therapeutic method for treating skin cancer. Because of its non-invasive nature, good aesthetic results, and targeted targeting of cancer cells, it is a viable alternative or supplement to standard therapies. Further advances in photosensitizing chemicals, light sources, and treatment procedures are likely to increase the efficacy and utility of PDT in skin cancer care as research proceeds, ultimately leading to better patient outcomes. Skin cancer's distinct traits and the skin's vulnerability to light irradiation make it an attractive target for PDT. Light therapy has been used to treat patients for over three millennia, extending back to ancient civilizations. PDT has transformed the area of light therapy by expanding on the old knowledge of light. Throughout history, civilizations such as the Egyptians, Greeks, and Romans recognized the medicinal benefits of sunshine and used it to treat wounds and skin ailments. Light has long been used as a therapeutic agent, with several civilizations and societies including light-based therapies in their medical traditions. Technological developments like lasers and PDT have accelerated the progress of light treatment. Laser therapy includes the accurate and regulated transmission of high-intensity light to particular tissues, allowing for the precise and controlled treatment of various illnesses. PDT, on the other hand, employs light-sensitive chemicals known as photosensitizers, which, when triggered by specific wavelengths of light, cause cellular damage and tissue death. Niels Finsen of Denmark made essential advances in the science of phototherapy, notably the application of light for medicinal reasons, in the late nineteenth century. Finsen showed that exposure to red light inhibited the production and discharge of smallpox pustules, suggesting a potential cure for this illness (Finsen, 19th century, Denmark) [1-3]. the use of photosensitizers and nanoparticles activated by UV light for cancer treatment, highlighting the potential of nanotechnology in improving diagnostics and treatment strategies at the nanoscale [4-7]. PDT produces localized photochemical reactions with light-absorbing photosensitizers. These reactions produce biological responses that are only active in the illuminated tissue regions. PDT is dominated by oxygen-dependent processes, which generate reactive oxygen species (ROS) that cause cytotoxicity and activate diverse cellular responses such as apoptosis or necrosis. In addition, non-oxygen-dependent photochemical processes, known as photo chemotherapy, such as DNA photo addition, have been established. One significant photochemotherapeutic technique is using psoralens in conjunction with ultraviolet A radiation to treat illnesses such as psoriasis and vitiligo and boost immunotherapy. Richard Lipson and his colleagues at the Mayo Clinic developed PDT, as we know it now, in the 1960s. They developed hematoporphyrin derivative (HPD) as a photosensitizer that particularly localized in tumors and generated fluorescence when activated by light. HPD showed considerable promise as a diagnostic tool compared to crude hematoporphyrin due to its ability to be supplied in smaller amounts. The processes underpinning the selective accumulation of photosensitizers such as HPD in tumors are complicated and remain unknown. Several reasons, however, contribute to this phenomenon, including the drugs' high vascular permeability, attraction for growing endothelial cells, and poor lymphatic outflow in tumor tissues. These properties are expected to contribute to photosensitizer preferential absorption and retention within tumor cells. PDT has progressed dramatically since its introduction, with photosensitizers such as HPD and the investigation of their selective accumulation in tumors. Although the particular processes involved in tumor targeting are not fully understood, continuing research strives to identify the underlying principles and use them to enhance diagnostic and therapeutic outcomes in cancer therapy [8-12].

Nanotechnology has introduced various nanoparticles for cancer diagnostics and treatment, with potential applications in physical, chemical, and biological behavior at the nanoscale size, particularly in PDT where nanomaterials can achieve passive and active drug delivery to tumor cells while minimizing toxicity to normal cells [13-15]. Developing PDT as a therapeutic option for skin cancer patients has been long and arduous. Von Tappeiner and Jesionek may trace its beginnings back to the 1903 investigations. However, it was not until 1972 that I. Diamond and colleagues proposed combining porphyrin's tumor-localizing and tumor-phototoxic capabilities in PDT. Initial in vivo investigations showed encouraging results. PDT, for example, has been shown to slow the development of gliomas implanted in rats, resulting in tumor suppression

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lasting 10-20 days. However, deeper parts of the tumors ultimately restarted growing, indicating that further progress is needed. 1975 Thomas Dougherty and his team announced terrific discoveries, which marked a watershed moment. They demonstrated that combining a photosensitizer termed HPD (hematoporphyrin derivative) with red light led to eliminating mammary tumor development in mice. This discovery highlighted PDT's potential efficacy in tumor eradication. Concurrently, J.F. Kelly and coworkers reported favorable outcomes using PDT. Light activation of HPD resulted in the elimination of bladder cancer in mice, proving the efficiency of this therapy method. These pivotal results in 1975 constituted a watershed moment in establishing PDT as a viable cancer therapy method. Eliminating tumors in animal models opened up new avenues for investigating PDT's applicability in human cancer patients. PDT has progressed since then, with continuous research focusing on optimizing photosensitizers, perfecting light activation procedures, and researching its efficacy in various forms of cancer. The 1975 achievements established the groundwork for subsequent research and clinical testing, eventually leading to the introduction of PDT into cancer therapy procedures. Overall, Diamond, Dougherty, Kelly, and their research teams proved the enormous promise of PDT in tumor eradication in the mid-1970s. Their ground-breaking discoveries set the path for further research, propelling the ongoing development and implementation of PDT as a viable treatment method in the battle against cancer [16-18]. Nanomaterials have various emerging applications at the nanoscale, particularly in clinical applications like PDT, due to their self-assembly, stability, specificity, drug encapsulation, and biocompatibility, allowing for passive and active strategies to increase drug concentration in tumors while minimizing toxicity in normal cells [19,20]. PDT has emerged as a viable therapeutic option for several types of skin cancer, one of the most common types of cancer worldwide. The frequency of skin cancer has been increasing in recent years. Traditional treatments, such as surgery, radiation therapy, and chemotherapy, have limits in efficacy and aesthetic outcomes. PDT is a non-invasive and precise method that uses photosensitizing chemicals, light activation, and oxygen to eliminate cancer cells while sparing healthy tissues. PDT was first used to treat various forms of cancer when it was first launched in the 1980s. J.S. McCaughey et al. undertook early investigations on PDT for oesophageal cancer in 1984, while O.J. Balchum et al. investigated its potential in treating lung cancer. A year later, Y. Hayata et al. looked at PDT as a therapy option for stomach cancer. These preliminary investigations showed excellent results, especially in early-stage patients, suggesting PDT for inoperable cases and patients with underlying health issues. PDT was later used to treat cancers such as breast cancer, gynecological tumors, intraocular tumors, brain tumors, head and neck tumors, colorectal cancer, cutaneous malignancies, intraperitoneal tumors, mesothelioma, cholangiocarcinoma, and pancreatic cancer. PDT's adaptability and potential as a treatment method are shown by the broad spectrum of cancer types in which it has been utilized. PDT is effective in various anatomical regions and tumor types, demonstrating its extensive relevance in oncology. These breakthroughs have increased therapy choices for people with previously difficult-to-manage malignancies. The effective use of PDT in various cancer types highlights its significance as an adjuvant or alternative therapy, mainly when traditional surgical intervention is not viable or has extra risks. PDT uses light exposure to selectively activate photosensitizers, resulting in a focused, less intrusive therapy strategy. Exploring PDT in various cancer types has cleared the path for more research and clinical trials. Ongoing research intends to enhance treatment results for a larger spectrum of patients by optimizing PDT procedures, selecting appropriate photosensitizers, and selecting appropriate photosensitizers. The growing body of data supports the continuing development and use of PDT as a helpful treatment method for cancer [21-30]. PDT employs a multi-step procedure. First, a photosensitizing chemical is given topically or injected into the patient and preferentially accumulates in cancer cells. When this agent is triggered by light of a specific wavelength, ROS are produced. ROS produced during PDT has direct cytotoxic effects, resulting in cancer cell death via various mechanisms such as oxidative stress, cellular structural destruction, and activation of apoptotic pathways. Furthermore, PDT can trigger an anti-tumor immune response, bolstering the body's defenses against cancer cells. Figure 1 depicts the standard steps in the PDT treatment. Semiconductor nanoparticles, specifically ZnO NPs, show potential in cancer treatment due to their high quantum yield, tunable emission, and ability to penetrate malignant cells when exposed to UV light, making them promising agents for photodynamic therapy (PDT) [31-34]. ZnO nanocrystals, which are semiconductors, have various applications in biomedical and bioimaging sensors, making them suitable as labeling agents due to their strong photostability and emission properties; they also have potential uses in UV, LED, and laser diodes for control of biological systems, monitoring, diagnosis, and tumor treatment in nanotechnology and nanomedicine [34-37].

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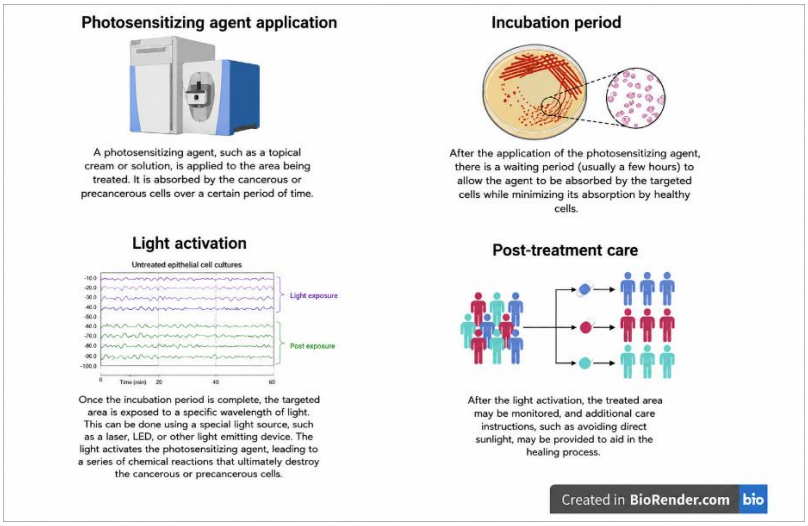

Figure 1. Steps of PDT.

Nanotechnology's properties of self-assembly, stability, specificity, drug encapsulation, and biocompatibility can be utilized in clinical applications like PDT to increase drug concentration in tumor cells while minimizing toxicity in normal cells [38-41]. PDT for tumor eradication involves direct damage to tumor and stromal cells leading to apoptosis, as well as microvascular injury and nonspecific immune activation; the therapeutic effect is based on the preferential retention of photosensitizer in tumor tissue and its reaction with biomolecules, and combining PDT with chemotherapy can increase photosensitizer availability at its intracellular site of action [42-45]. Bibliometrics and visualization approaches have been recognized as critical tools for identifying developing infectious disease outbreaks and assessing scientific research [46,47]. This awareness is essential today as massive volumes of data are created and exchanged [46,48,49]. Bibliometrics is widely used to examine scientific research's quantitative and qualitative features in various domains, including infectious illnesses [50]. The data emphasize a comprehensive evaluation of Multicriteria decision analysis (MCDA) in the healthcare industry, including a complete investigation of research and bibliometric analysis [51]. The examination will concentrate on many critical issues. To begin, it will study the production of publications throughout time to recognize the progress and advancement of research in the given sector. Furthermore, the study will examine how publications are spread across different journals to discover the critical pathways for PDT research on skin cancer. The study will undertake a citation analysis to discover the most prominent papers and writers in the area, assisting in identifying research collaborations and disseminating information. Furthermore, the analysis will highlight the geographic distribution of research, identifying the leading nations and universities in skin cancer PDT research. According to the review findings, MCDA has been used in various healthcare situations, utilizing various methodological methodologies [52]. Decision-making procedures in healthcare sometimes entail the consideration of several criteria or considerations, which can be complicated. MCDA offers a methodical technique for dealing with such difficulties by including several criteria, frequently of disparate types, into a decision-making framework. This method enables decision-makers to simultaneously assess and evaluate several choices based on multiple criteria.

The in-depth examination of MCDA in healthcare includes fully explaining its applications, techniques, and outcomes. It investigates how MCDA has been used in diverse healthcare situations, demonstrating its flexibility and versatility in tackling complex decision issues. The research considers a wide range of methodological strategies used in MCDA, illustrating the diversity of methodologies used in healthcare decision-making. Furthermore, the study and bibliometric analysis thoroughly review the available literature on MCDA in healthcare. The study seeks to discover trends, patterns, and research orientations within the subject by evaluating published publications and employing bibliometric tools. This study aimed to thoroughly examine the papers on PDT in skin cancer that were indexed in the Web of Science (WoS) database. The study used the quantitative technique to examine the quantitative and qualitative components of scientific research in the field of MCDA in healthcare. The bibliometric analysis was aided by using Bibliometrix, an R tool, and the web-based interface Biblioshiny and VOSviewer software. This technique gave valuable insights into the

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present status of the discipline and indicated prospective topics for future research [53,54]. This is the first research to examine publication trends in PDT for skin cancer. The primary goal of this study was to identify the major research sites and institutions that are actively involved in the field of PDT in skin cancer. This study provides valuable insights into this sector's national and institutional research initiatives by analyzing bibliometric data. Furthermore, data visualization and analysis using bibliometric approaches might help examine the historical trajectory of research output in PDT for skin cancer. It also makes identifying potential future research areas easier and encourages collaboration among scholars and organizations [55,56].

2. METHODS AND MATERIALS

Bibliometric studies offer a comprehensive study that offers a unique perspective. The R package's bibliometrics feature is designed for quantitative Scientometrics and informatics [57]. Furthermore, bibliometric technologies make it possible to organize and analyze vast amounts of historical research data to glean insightful information from the archive. Bibliometric analysis and meta-analysis use quantitative methods that minimize or eliminate biases. This contrasts with systematic literature reviews, which frequently rely on qualitative approaches and can be vulnerable to interpretation biases from scholars with different academic backgrounds [58].

In order to look at current trends in research on photodynamic therapy for skin cancer, this study used bibliometric analysis. A thorough, open, and reproducible quantitative and statistical evaluation of publications is known as bibliometric analysis. Content analysis and descriptive analysis are two crucial methods used in bibliometric analysis. By carefully evaluating several articles and journal indices, the descriptive analysis evaluates the author's and source papers' impact. In contrast, content analysis reveals the conceptual frameworks of specific disciplines through keyword and citation analyses, making it possible to spot new subjects, themes, and study areas.

Numerous databases, including Scopus, WoS, Dimensions, Cochrane Library, Lens, and PubMed, allow users to import bibliographic data. These databases each have unique characteristics and capabilities. WoS and Scopus are currently the most widely used literature databases in numerous academic domains [59,60]. We used the WoS database in this study because of its enormous collection of publications and detailed citation information [61]. The WoS database is a comprehensive resource that allows researchers to explore and evaluate a wide range of publications, including research articles, patents, clinical trials, and policy papers. Using the following criteria, we narrowed our search to article titles, abstracts, and author keywords: PDT (Photodynamic Therapy) AND (skin) AND (carcinoma OR cancer). Biochemistry, genetics and molecular biology, computer science, social sciences, pharmacology, toxicology and pharmaceutics, immunology and microbiology, and medicine were all covered in this research. To narrow our search, we chose a publication date range of January 2000 to July 23, 2023. The data was downloaded on July 23, 2023, yielding 2890 publications. We omitted comments, editorials, letters, conference papers, book chapters, and articles or reviews published on preprint websites.

We extensively examined and evaluated published data explicitly focusing on PDT for skin cancer. We excluded publications that discussed PDT but emphasized other forms of therapy. We identified a dataset of 1654 scientific papers published between January 2000 and July 23, 2023, by applying these specific inclusion and exclusion criteria. This dataset served as the foundation for the bibliometric analysis conducted in our study. We employed a search method illustrated in **Figure 2** to locate relevant articles from the WoS database. We downloaded the complete set of bibliographic data from WoS in .txt format. Subsequently, we installed and loaded the Bibliometrix R package in R Studio. For the convenience of non-programmers, we accessed the web application Biblioshiny by typing Biblioshiny () in the R console. Biblioshiny, which grants access to the Bibliometrix package, offers a range of tools for conducting thorough bibliometric analysis [62].

Our study focused on PDT for skin cancer, where we extensively examined and evaluated published data. We carefully excluded publications that discussed other forms of therapy alongside PDT. By applying these inclusion and exclusion criteria, we identified a dataset of 2690 scientific papers published between January 2000 and July 23, 2023. This dataset served as the basis for the bibliometric analysis conducted in our study.

We obtained the complete set of bibliographic data from WoS in .txt format and proceeded to install and load the Bibliometrix R package in R Studio. For the convenience of non-programmers, we accessed the web application Biblioshiny by executing the command Biblioshiny in the R console. Biblioshiny, which provides access to the Bibliometrix package, offers a variety of tools to facilitate comprehensive bibliometric analysis. VOSviewer, Biblioshiny, Microsoft Word, and Excel were among the many tools used to handle, analyze, and visualize the data.

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With regard to photodynamic treatment and skin cancer research worldwide, the following questions were the focus of this study:

- To what extent has photodynamic treatment been studied for skin cancer research worldwide, and how has it evolved over time?
- What kind of influence has this study had?
- Who is working with whom on photodynamic therapy research for skin cancer worldwide and how are they collaborating?
- Which worldwide institutions, authors, and publications are most involved in photodynamic treatment research for skin cancer?
- What are the most popular terms and topics in worldwide photodynamic treatment research for skin cancer?
- What are the most research area being investigated worldwide for photodynamic treatment for skin cancer?
- How do the links between authors, journals, and nations emerge from the cited references in the worldwide study on photodynamic treatment for skin cancer?
- Which international funding agencies support photodynamic therapy for the study of skin cancer?

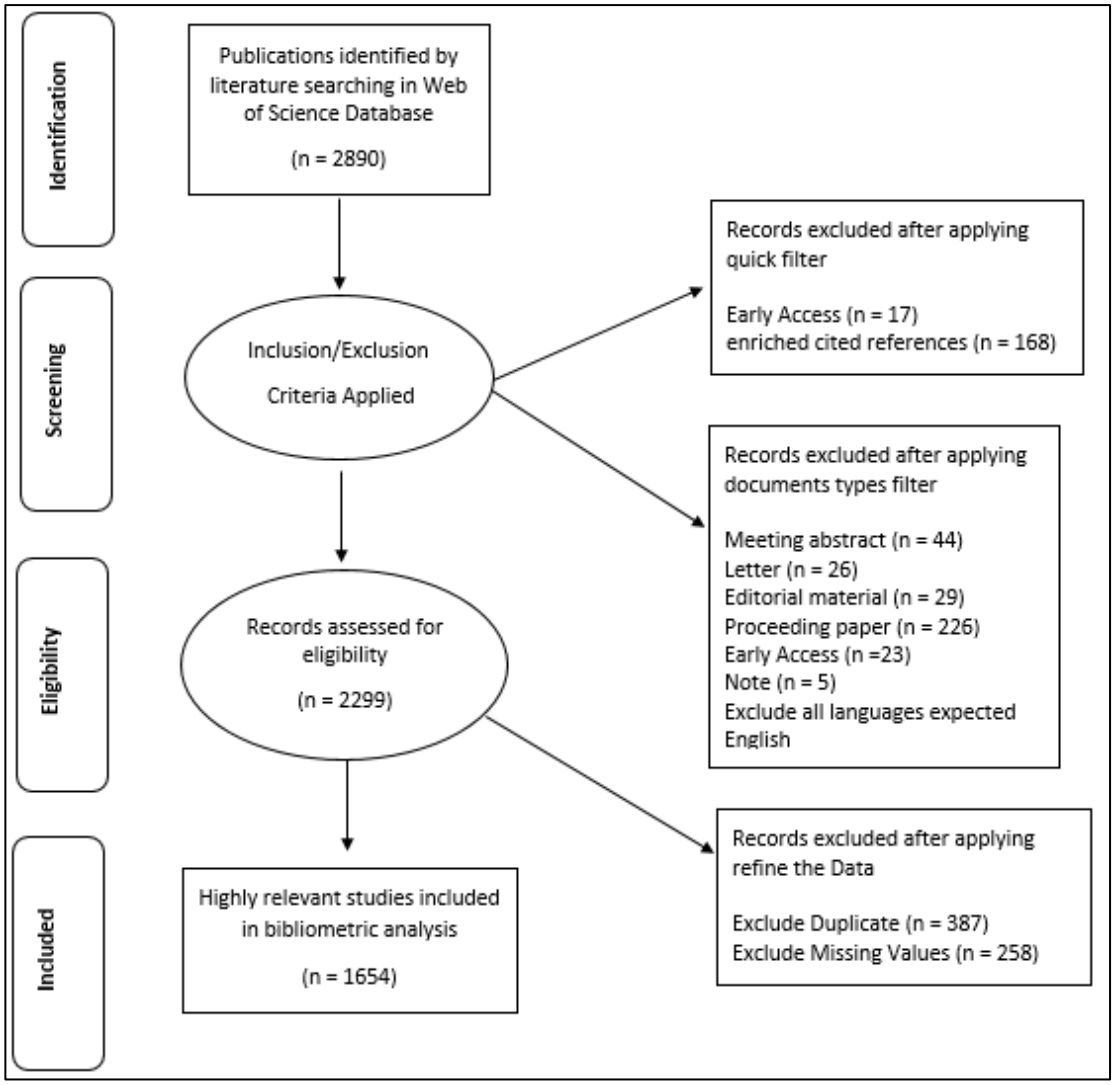

Figure 2. Flow diagram of literature selection and screening in this study

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Table 1 provide overview of tools and software, which use for this study. Creating maps from text, bibliographic, or network data is the main use of VOSviewer (version 1.6.19). Bibliographic coupling between nations, journals, authors, and keywords is identified, and it facilitates map exploration and visualization. With an emphasis on activities like tracking citation bursts and analyzing topic progression, Biblioshiny (version 4.1) provides a web interface for bibliometrix. A powerful spreadsheet programme for data organization and analysis, Microsoft Excel (2016 edition) is used for a variety of purposes, including comprehending citation structures, following the development of publications and citations, and locating active authors and organizations.

Table 1. Tools and software used in data visualization and processing.

Software/Tools	Description of Software	Data Analysis
VOS viewer (version 1.6.19)	A tool for making maps based on text, bibliographic, or network data is called VOSviewer. The programme facilitates map exploration and visualization as well.	Bibliographic coupling countries (figure 13), journals (figure 12), and authors (figure 11), All Keywords (figure 8), Author Keywords (figure 9) were identified by VOS viewer
Biblioshiny (version 4.1)	An online interface for bibliometrix is offered by the software biblioshiny.	Citation Bursts (figure 7), thematic evolution (figure 10)
Microsoft Excel (2016 version)	Spreadsheets are used in Microsoft Excel, a powerful programme designed by the company to organize and analyze data using functions and formulae.	Evolution of publications and citations (figure 3), Citation structure (figure 5), active organizations (table 5), active authors (table 4), top funding bodies (figure 14), Authorship patterns (figure 6), Active journals (table 3)
Microsoft Word (2016 version)	Microsoft Word is a word processing programme that may assist users in creating a variety of document.	Flow diagram (figure 1)

3. RESULT

3.1 Main Information

Table 2 contains numerous statistics and facts on PDT in the context of skin cancer research. The data spans from 2000 to 2023 and includes 1654 documents from 470 sources. The data's yearly growth rate is 4.44%, demonstrating a significant increase in research over time. The documents in this collection are 8.24 years old on average, indicating that the data comprises both recent and older research. The average number of citations per document is 30.14, demonstrating the scientific community's degree of impact and recognition. Furthermore, the dataset has many references (54,082), illustrating the breadth of study and knowledge integration. There are 3,367 keywords plus (identified using a specific system or identification) and 3,545 author's keywords (supplied by the authors themselves) that encapsulate the essential topics and issues the research covers. There are 6804 authors linked with the texts, illustrating the variety of scholars contributing to the topic. Among these writers, 33 have written single-authored works, but the bulk (37) is the product of author cooperation, with an average of 5.82 co-authors per document. Furthermore, roughly 21.7% of these co-authorships are multinational partnerships, emphasizing the transnational aspect of PDT for skin cancer research. Finally, the dataset's document types include 1,256 articles and 398 reviews, reflecting the many research outputs and analyses undertaken.

Table 2. Overview of Data.

Description	Results
Main Information About Data	
Timespan	2000:2023
Sources (Journals, Books, etc)	470
Documents	1654
Annual Growth Rate %	4.44
Document Average Age	8.24

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Average citations per doc	30.14
References	54082
Documents Content	
Keywords Plus (ID)	3367
Author's Keywords (DE)	3545
Authors	
Authors	6804
Authors of single-authored docs	33
Author Collaboration	
Single-authored docs	37
Co-Authors per Doc	5.82
International co-authorships %	21.7
Document Types	
Article	1256
Review	398

3.2 Publication Growth Annually

Figure 3 depicts the number of publications published annually from 2000 to 2023 about PDT in treating skin cancer. Based on the data, it is clear that the number of publications has changed over time. Early in the new millennium, there was a general increasing trend indicated by the number of publications, which began at 21 in 2000 and progressively climbed to 68 in 2011. There was a brief decline to 61 publications in 2012. From 2013 onwards, there was a discernible rise in the annual number of publications; in 2016 and 2017, this number reached an all-time high of 92 and 104, respectively. After that, the number of publications fluctuated yearly even if it stayed comparatively high. An overview of the publishing patterns in the designated field is given by this dataset, which shows times of growth, fluctuations, and changes for research produced throughout time. More study is needed to determine the underlying causes of these variations in publication numbers; potential suspects include worldwide events, burgeoning trends, and research financing, among other things that may have an impact on the field's publishing rates.

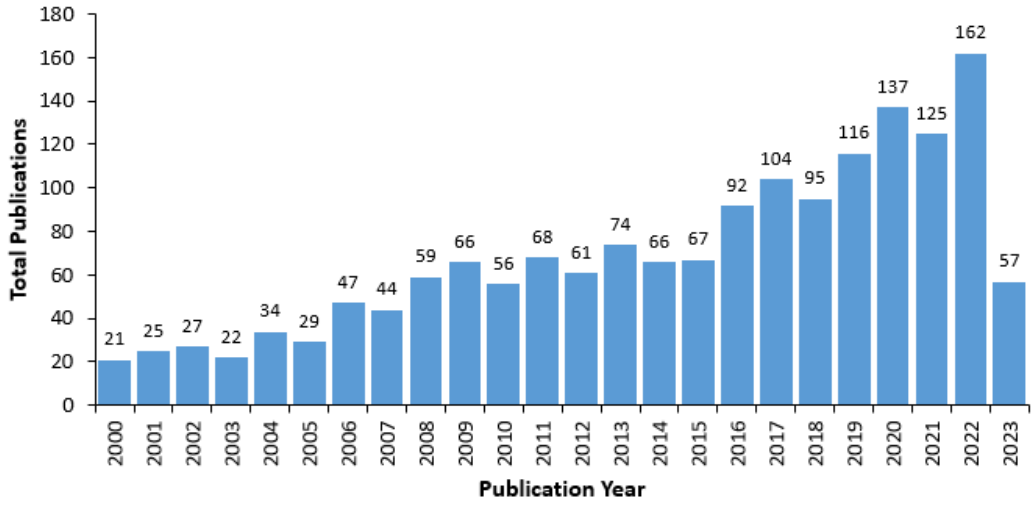

Figure 3. Annual Publications Growth.

The Sanky plot, the three-field plot, was used to visualize the links between nations, authors, and keywords in photodynamic treatment (PDT) for skin cancer research articles. Colorful rectangles represented these elements, and the height of each rectangle denoted the total number of connections linked with that element. A giant rectangle represented an element with more connections. Figure 4 depicted Sankey diagrams displaying the top ten most prolific nations and authors, highlighting their significant contributions to PDT for skin cancer research. Notably,

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writers from the United Kingdom, Germany, and Italy performed significant roles in investigating PDT for skin cancer, concentrating on various critical factors. The Sankey diagram efficiently illustrated the distribution of amounts across several categories, such as nations, authors, and keywords. The thickness of the connections or linkages represented the substantial information flow between certain data groups.

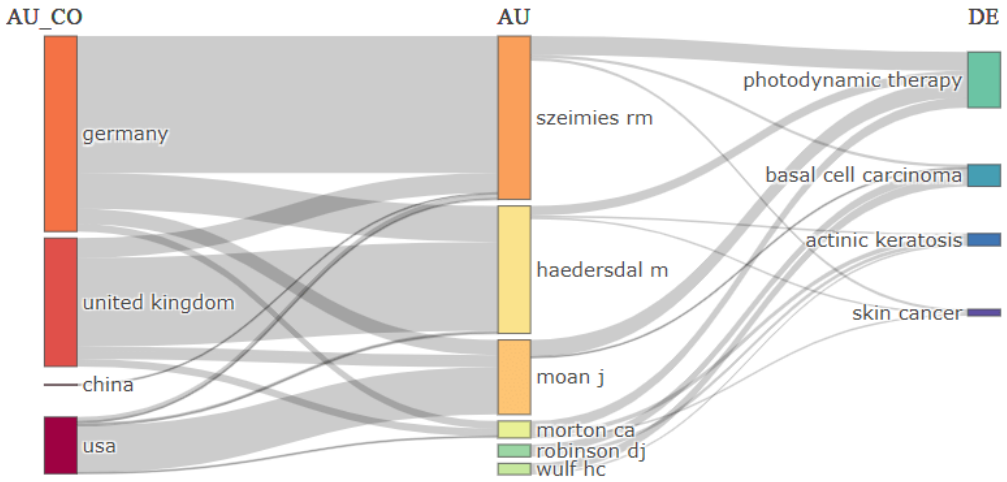

Figure 4. Relationship found in PDT for skin cancer research between countries, authors, keywords.

3.3 Research Impact

Data on publications and their citations over a number of years are show in the figure 4. With years ranging from 2000 to 2023, the material looks to be arranged chronologically. The table displays the quantity of publications (TP) and total citations (TC) linked to those publications for each year. These figures provide information on the effect and productivity of publications or research in a particular year. In 2023, there were 57 publications in total, but only 38 citations for those papers overall. This implies that the scholarly or research community has not yet given that year's research or publications as much attention or recognition. In contrast, the 59 papers from 2008 earned a sizable amount of citations, totaling 4018. This would suggest that studies conducted in 2008 have had a substantial and enduring influence on the area. The information may be used to monitor changes over time in the productivity and effect of research. By counting the number of citations, it may also be used to determine which years had a large publishing volume and which years had articles that were very significant. Institutions and researchers to evaluate the effects of their work and to decide on the best course for future study frequently use such information.

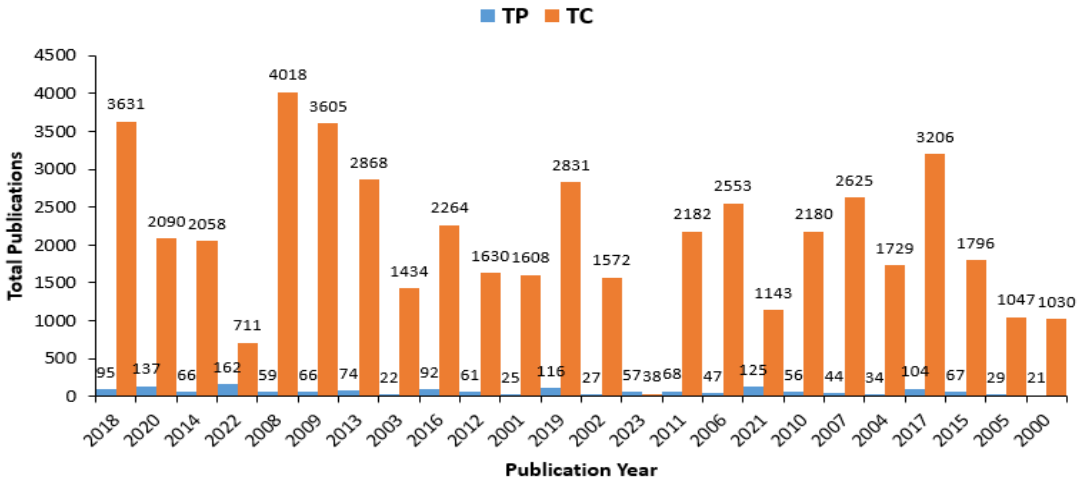

Figure 5. Research Impact.

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3.4 Patterns of Authorship

Figure 6 for different writers that displays the TC and TP. The writers are numbered 1 through 31, and each row in the table represents a distinct author. The TP that each author has varies greatly; it might be as low as one publication or as high as 254 publications. This implies that the writers' output of scholarly writing varies at different rates. There is also a significant variation in the TC, with some writers having relatively few citations (e.g., 10) and others having a significant amount (e.g., 7592). An author's effect and influence may frequently be determined by counting the citations to their work. With 245 and 254 publications, respectively, authors 4 and 5 have the most. These writers have added a great deal to the corpus of scholarly writing. A significant number of citations (7592 and 7134, respectively) is also included for authors 4 and 5, indicating that their work has had a significant influence on their area. With only one publication between them, authors 16, 18, 21, 22, 23, 27, and 28 have comparatively low levels of output. These writers' varied citation counts indicate differing levels of influence. Despite the fact, that Authors 4 and 5 have many citations, it is crucial to take the citation to publication ratio into account. An author's work can be judged for its quality and impact by the quantity of citations it receives each publication.

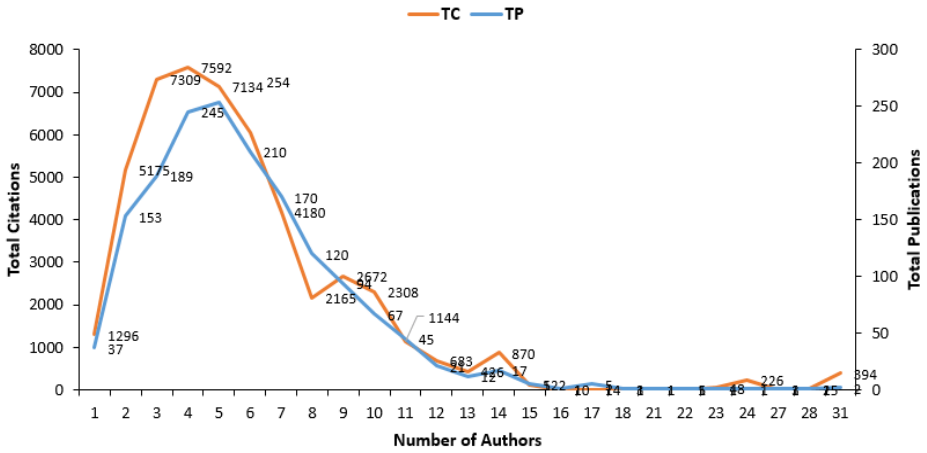

Figure 6. Authorship Pattern.

3.5 Highly Productive and Widely Cited Journals in Academic Publishing

Table 3 lists publishers, countries of origin, TP, TC, citation impact (CI), quartile (Q), and impact factor (IF) for a variety of dermatological and related medical journals. Wiley publishes both the British Journal of Dermatology and Lasers in Surgery and Medicine; the former has a higher CI and IF with 56 publications, while the latter has 63 publications. The Netherlands' Elsevier article, Photodiagnosis and Photodynamic Therapy, has a Q2 quartile and a significant TC. Elsevier journals with a Q1 quartile and a lower TP, but a high IF, demonstrate a substantial impact on the subject, such as Biomaterials. To evaluate the relative significance and influence of these publications in the field of dermatology and allied disciplines, professionals and researchers need to have access to this data.

Table 3. Sources Analysis

Journal	Publisher	CU	TP	TC	CI	*Q*	IF
British Journal of Dermatology	Willey	UK	56	5532	98.78	Q1	3.46
Lasers in Surgery and Medicine	Willey	USA	63	2067	32.8	Q1	2.86
Photodiagnosis and Photodynamic Therapy	Elsevier	Netherlands	167	3224	19.3	Q2	3.41
Journal of Photochemistry and Photobiology B: Biology	Elsevier	Netherlands	57	2221	38.96	Q1	5.4
Photodermatology, Photoimmunology & Photomedicine	Wiley-Blackwell	UK	41	1262	30.78	Q2	1.56

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Acta Dermato-Venereologica	Medical Journals/Acta D-V	Sweden	31	944	30.45	Q1	2.07
Journal of the American Academy of Dermatology	Elsevier	USA	32	1923	60.09	Q1	3.2
Journal of the European Academy of Dermatology and Venereology	Wiley-Blackwell	USA	20	1144	57.2	Q1	3.74
Lasers in Medical Science	Springer	UK	35	1052	30.05	Q2	2.57
Biomaterials	Elsevier	UK	16	869	54.31	Q1	13.74

3.6 Most Relevant Author

Ten writers, their research statistics, and the number of years they were actively involved are included in the **Table 4**. According to their CI, which calculates the typical number of citations their work obtains, the writers are arranged in descending order. Having published 24 publications between 2006 and 2022, Dr. Haedersdal M is in the top place with a confidence interval of 46.66. Drs. Tedesco Ac and Moan J have comparable high confidence intervals and are placed second and third, respectively. With 2051 TC and a smaller confidence interval, Dr. Morton Ca has the greatest total of any author, suggesting a considerable body of work from 2000-2021. Additionally, for each author's research contributions throughout the designated time period, the table gives information on the Starting Year (SY), Ending Year (EY), and Active Year (AY).

Table 4. Author analysis.

Rank	Author	TP	TC	CI	SY	EY	AY
1	Haedersdal M	24	1120	46.66	2006	2022	16
2	Tedesco Ac	19	694	36.52	2003	2022	19
3	Moan J	19	777	40.89	2001	2010	9
4	Morton Ca	16	2051	128.18	2000	2021	21
5	Woolfson Ad	15	492	32.8	2004	2010	6
6	Donnelly Rf	18	494	27.44	2004	2022	18
7	Mccarron Pa	15	431	28.73	2004	2010	6
8	Wulf Hc	18	672	37.33	2003	2022	19
9	Ibbotson Sh	15	682	45.46	2002	2019	17
10	Moseley H	14	1095	78.21	2002	2017	15

3.7 Most Relevant Affiliations

Table 5 shows the number of publications published by various academic institutions or research centers on PDT in the context of skin cancer. With a TP of 97, the "University of Sao Paulo" has 97 research publications published. Additionally, their TC of 1686 indicates that 1686 citations overall for their study. Their CI is 17.38, which indicates that each of their papers get 17.38 citations on average. Brazil is the location of this establishment. With a CI of 32.55, the "University of Copenhagen" has a TP of 49 and a TC of 1595. This implies that their research is based in Denmark and that their articles are often referenced. With a TP of 25 and a TC of 1033, the "Harvard Medical School" in the US has a high confidence interval of 41.32, suggesting a notable influence on research. To evaluate these institutions' academic and research standing in their respective disciplines, the table offers a quick overview of their research production and influence across various national borders. This number of publications reflects these institutions' continued efforts and dedication to scientific discovery and academic achievement in PDT for skin cancer.

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Table 5. Most dominant affiliation in research of PDT for skin cancer

Affiliation	TP	TC	CI	CU
University of Sao Paulo	97	1686	17.38	Brazil
University of Copenhagen	49	1595	32.55	Denmark
Roswell Park Comprehensive Cancer	39	802	20.56	U.S.A
University of Dundee	35	1594	45.54	Scotland
Case Western Reserve University	31	1038	33.48	U.S.A
Wroclaw Medical University	29	447	15.41	Poland
National Taiwan University	26	416	16	Taiwan
Queen's University Belfast	26	555	21.34	UK
Harvard Medical School	25	1033	41.32	U.S.A
University of Manchester	21	1106	52.66	UK

3.8 Strongest Citation Bursts of Authors

The writers are included in the Figure 6, with a particular emphasis on three of them: WANG XL, HAEDERSDAL M, MOAN J, and TEDESCO AC in addition to DONNELLY RF. The data set spans the years 2001 through 2023. The year of publication for each author is followed by the total count (abbreviated "TC") of his or her publications in that year, as well as the specific count of publications for that year. HAEDERSDAL M has been actively publishing from 2006 to 2022, with a significant peak in 2016 (6 publications), whereas DONNELLY RF has publications from 2004 to 2022, with the largest publication count in 2008 (3 publications). TEDESCO AC published from 2003 to 2022, with the most publications in 2017 (3 publications), while MOAN J published from 2001 to 2010, with the greatest number of publications in 2005 (98 publications). Finally yet importantly, WANG XL published continuously from 2009 to 2023, with the biggest number of publications occurring in 2022 (6 publications). With a focus on their most productive years and the overall number of articles they have produced within the given timeframe, this figure 6 provides a brief summary of these writers' publishing habits throughout time.

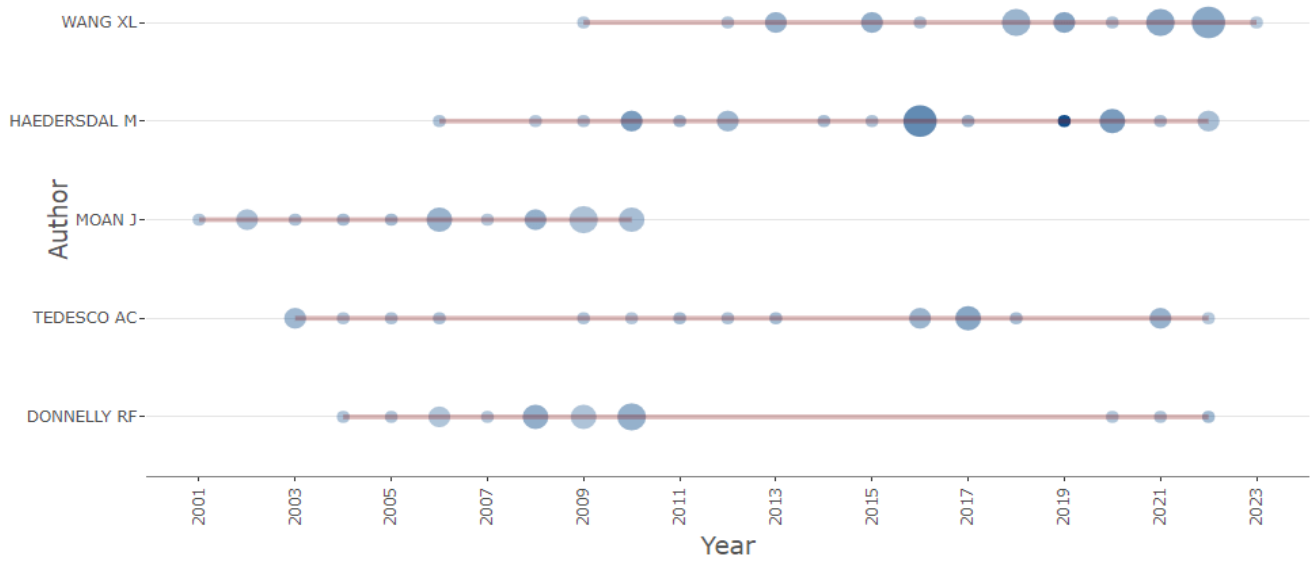

Figure 7. Citation Bursts

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3.9 Thematic Evolution and Keywords

Figure 8 seems to be a grouping of several words and ideas associated with PDT in relation to the management of skin cancer. The words are divided into four unique clusters, denoted by a distinctive color for each. Cluster 1 (Red): This cluster appears to be centered around various phototherapy treatments and associated terminology. This place makes extensive use of the phrase "photodynamic therapy", a therapeutic approach that targets and kills cancer cells using light and photosensitizing chemicals. Another method that uses heat produced by light to cure cancer is called photothermal treatment. This cluster may possibly be investigating different technology and treatment approaches utilized in PDT for skin cancer. Cluster 2 (Blue): The usage of certain chemicals and compounds in PDT seems to be the focus of this cluster. Agents used in PDT include 5-aminolevulinic acid (5-ALA) and methyl aminolevulinate, which sensitize cells to light and increase their susceptibility to damage. A particular kind of PDT that uses 5-aminolevulinic acid is called ALA-PDT. It's possible that this cluster is highlighting how crucial these substances are to the management of skin cancer. Cluster 3 (Green): It appears that this cluster is concentrated on various forms of skin cancer and associated ideas. There are several forms of skin cancer and precancerous diseases, including squamous-cell carcinoma, basal cell carcinoma, actinic keratosis, and cutaneous squamous cell carcinoma. Skin cancer is treated surgically using a method called Mohs micrographic surgery. This cluster probably covers the variety of skin cancer kinds and pertinent medical procedures. Cluster 4 (Yellow): Research on PDT and skin cancer may be connected to this cluster's larger context. Autophagy, signalling pathways, and metastasis are important components of skin cancer development and biology. One biological function that may affect how well cancer treatments work is autophagy. This cluster could be investigating the fundamental processes and variables influencing PDT results in the management of skin cancer. This figure offers a structured perspective of the several elements associated with PDT in skin cancer, such as chemical compounds, forms of skin cancer, therapy modalities, and basic biological processes. These clusters aid in the comprehension of the complex treatment strategy and interrelated elements of PDT for skin cancer by scientists and healthcare practitioners.



Figure 8. All Keywords

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Figure 8 shows to be a grouping of words and ideas associated with PDT in relation to the management of skin cancer. The phrases inside each cluster appear to be classified according to their applicability to particular facets of PDT for skin cancer, and each cluster is represented by a distinct color. Cluster 1 (Blue): It appears that the fundamental ideas of PDT are at the centre of this cluster. The main phrase in this cluster is PDT, a type of treatment that uses photosensitizing drugs to target and kill cancer cells when they come into contact with certain light wavelengths. A more general word for a variety of light-based medical interventions is phototherapy. Hypericin is another photosensitizing drug, and bodipy is most likely the photosensitizer utilized in PDT. It seems that the core ideas of PDT for skin cancer are the emphasis of this cluster. Red Cluster 2: The phrases in this cluster appear to be related to various forms of skin cancer. Actinic keratosis and basal cell carcinoma are two particular forms of skin cancer or precancerous diseases. Another kind of skin cancer is called squamous cell carcinoma. This cluster could highlight how crucial it is to comprehend and use PDT to treat these various forms of skin cancer.

Cluster 3 (Orange): The agents and chemical components of PDT for skin cancer appear to be the main focus of this cluster. Compounds such as 5-ALA and its derivative methyl aminolevulinate can be administered topically to light-sensitize cells. PDT uses a photosensitizing chemical called protoporphyrin IX. Since oral cancer may damage the skin in the mouth cavity, the inclusion of oral cancer suggests that these substances may be utilized to treat it. This cluster may cover the pharmacological and chemical elements of PDT. Cluster 4 (Green): This cluster includes several more ideas on PDT in skin cancer. Included are photosensitizers with dual medicinal and diagnostic use, such as indocyanine green and theranostics. The use of heat-based therapies in addition to PDT is suggested by the mention of hyperthermia and field therapy. One potential unique approach to PDT agent delivery is the dissolution of microneedles. In the context of PDT for skin cancer, this cluster seems to encompass a variety of cutting-edge and novel technology and therapeutic approaches.

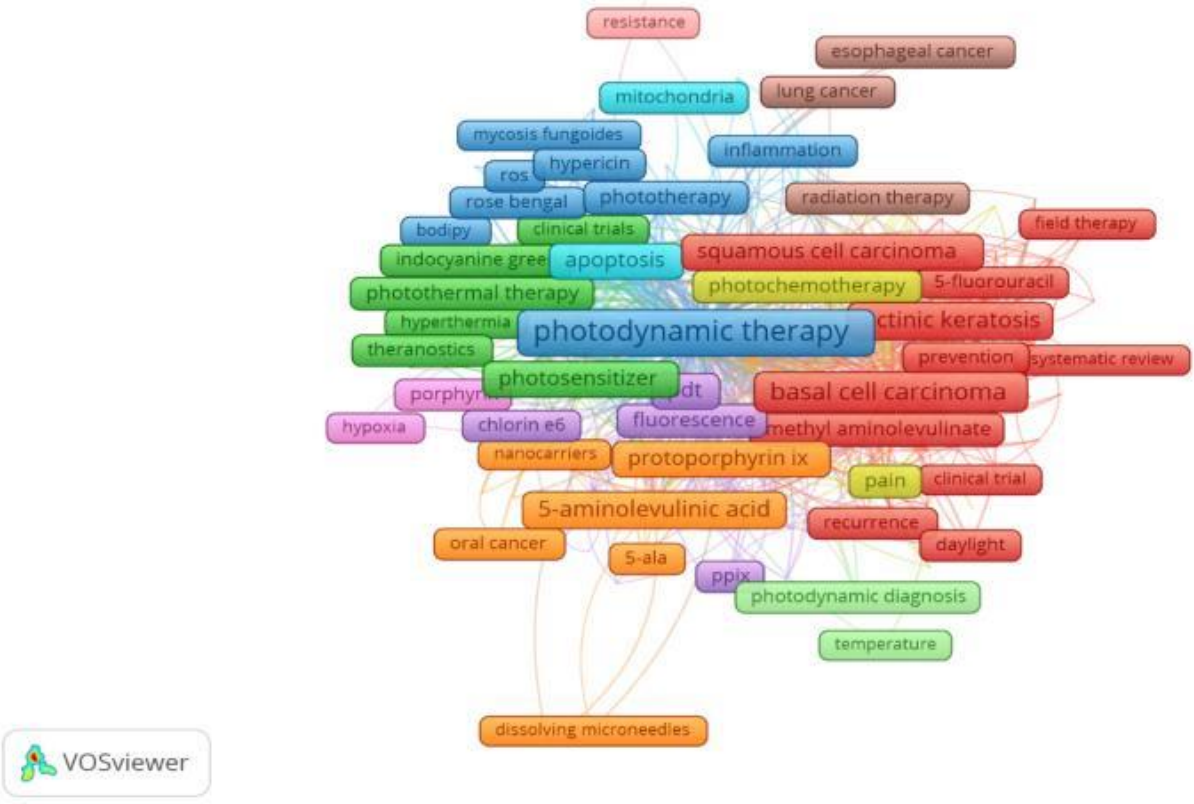

Figure 9. Author Keywords

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The information in the Figure 9 relates to photodynamic therapy, a medical intervention that is used to treat a number of illnesses, most prominently skin cancer. "Photodynamic therapy" was the most common keyword in the sample, with 974 occurrences. With 155 incidences, "skin cancer" may be closely related to photodynamic treatment. With 122, 96, and 91 instances, respectively, the phrases "5-aminolevulinic acid," "protoporphyrin ix," and "aminolevulinic acid" are associated with the particular compounds utilized in this treatment. The term "fluorescence" appears 49 times, indicating that it is used in the process. Furthermore, the 39 instances of "dermatology" denote the medical profession that treats skin-related conditions. As components of the therapeutic procedure or the afflicted area, "5-aminolaevulinic acid," "methyl aminolevulinate," and "skin" are also referenced 38 times, highlighting their significance to photodynamic therapy. Together, these phrases create a cluster that is referred to as "photodynamic therapy," highlighting their crucial function in this medical treatment.

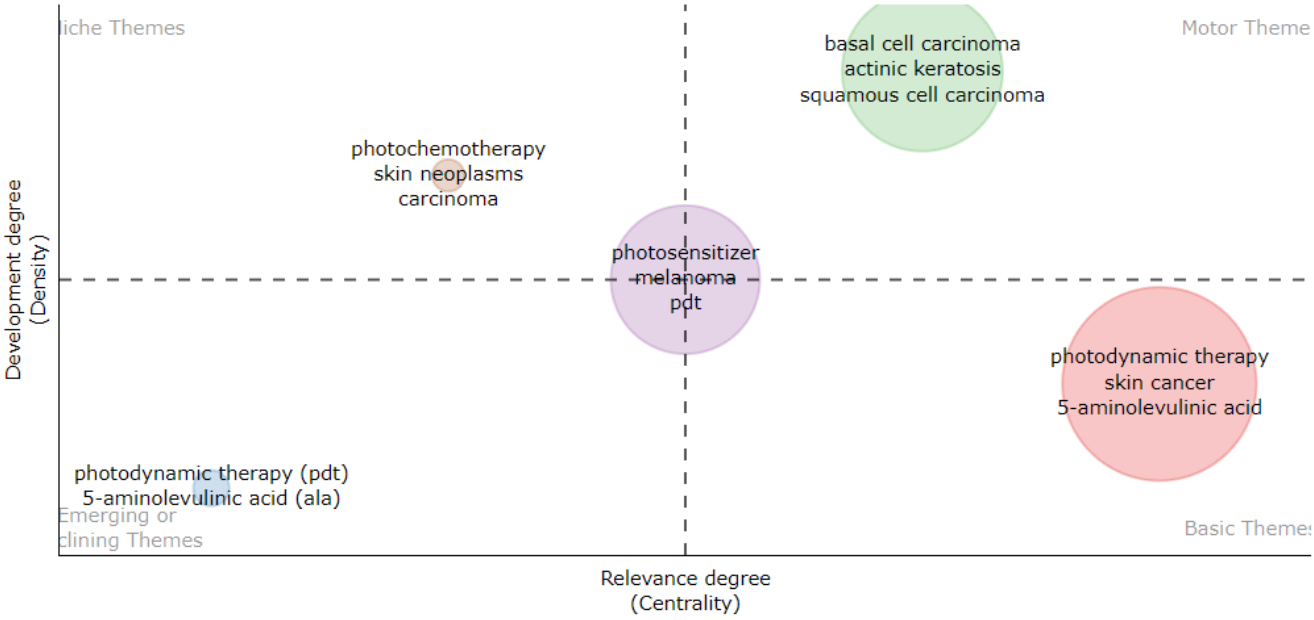

Figure 10. Thematic Map

3.10 Research Area

In a dataset of 1654 items, the Table 6 presents different research topics and their proportions. Dermatology is by far the greatest research topic among them, with 355 cases and 21.46% of the entries. It would appear from this that the dataset has a substantial emphasis on skin-related studies. With 200 cases, Oncology comes in second place with 12.09% of the records. This suggests that there is a wide body of research on cancer research. With 137 items, biochemistry and molecular biology account for 8.28% of the collection. The research on the basic molecular aspects of the biological sciences is highlighted in this area. With 111 entries, pharmacology and pharmacy make up 6.71% of the dataset, highlighting the significance of research on pharmaceuticals and medications. With 105 entries, surgery ranks as the fifth-largest category, accounting for 6.35% of the dataset. This indicates a substantial body of research in the surgical medicine subject. With 98 entries, chemistry makes up 5.93% of the dataset, suggesting a significant amount of chemical research. There is a notable concentration on physics-related research fields in biophysics (4.89% and 81 records) and optics (4.66% and 77 records). The dataset's proportions of 3.45% for Materials Science and 3.69% for Engineering highlight the importance of technical and material-related research. With a focus on dermatology, oncology, and biochemistry and molecular biology, this dataset represents a wide range of study topics and offers insights on the distribution of research interests within it.

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Table 6. Research Area.

Research Areas	Record Count	% of 1654
Dermatology	355	21.46
Oncology	200	12.09
Biochemistry Molecular Biology	137	8.28
Pharmacology Pharmacy	111	6.71
Surgery	105	6.34
Chemistry	98	5.92
Biophysics	81	4.89
Optics	77	4.65
Engineering	61	3.68
Materials Science	57	3.44

3.11 Authors, Journals, and Countries Bibliographic Coupling

A bibliography of writers is depicted in the Figure 11, divided into four separate groups and given a distinctive color for reference. Those in Cluster 1, which is indicated in red, include Am Soler, Rolf-Markus Szeimies, and Michael Landthaler. Cluster 2, represented in green, includes individuals such as Michael R. Hamblin, H. Mukhtar, and Elma D. Baron. Names like Dominic J. Robinson, Ellen R. M. de Haas, and Henricus J. C. M. Sterenborg are included in Cluster 3, which is show in yellow. Lastly, people like Edward V. Maytin, Tayyaba Hasan, and M. Shane Chapman are part of Cluster 4, which is show in blue. These groups of names may indicate hierarchical, thematic, or collaborative links among the persons mentioned inside each cluster. These clusters are probably related to a particular study or organizational environment.

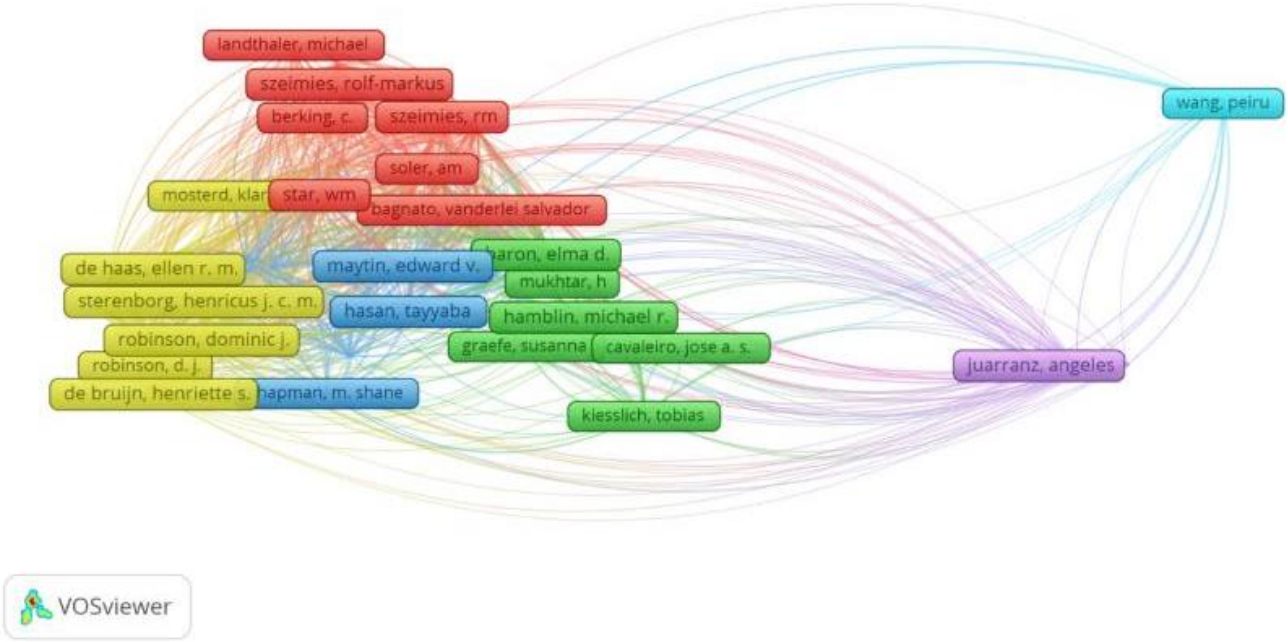

Figure 11. Bibliography Coupling of Authors.

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Several journals are grouped into two separate clusters, designated as Cluster 1 (Red) and Cluster 2 (Green), in the **Figure 12** presentation. These clusters appear to be arranged according to the shared topics and themes among the journals that make up each cluster. The journals in Cluster 1, which is highlighted in red, are mostly concerned with biomedical optics and related subjects. These publications, which include "Photochemistry and Photobiology," "Lasers in Surgery and Medicine," and "Journal of Biomedical Optics," are probably going to publish studies and papers about the application of optical technologies and methods in biological and medical contexts. Topics pertaining to dermatology and skin care appear to be the focus of Cluster 2, which is show in green. Publications with titles such as "European Journal of Dermatology," "British Journal of Dermatology," and "Journal of the American Academy of Dermatology" demonstrate the focus of this cluster on research in dermatology and related fields. The figure aids in the classification of these journals into discrete study subjects, which facilitates readers' and researchers' identification of papers pertaining to their particular fields of interest, such as dermatology or biomedical optics.

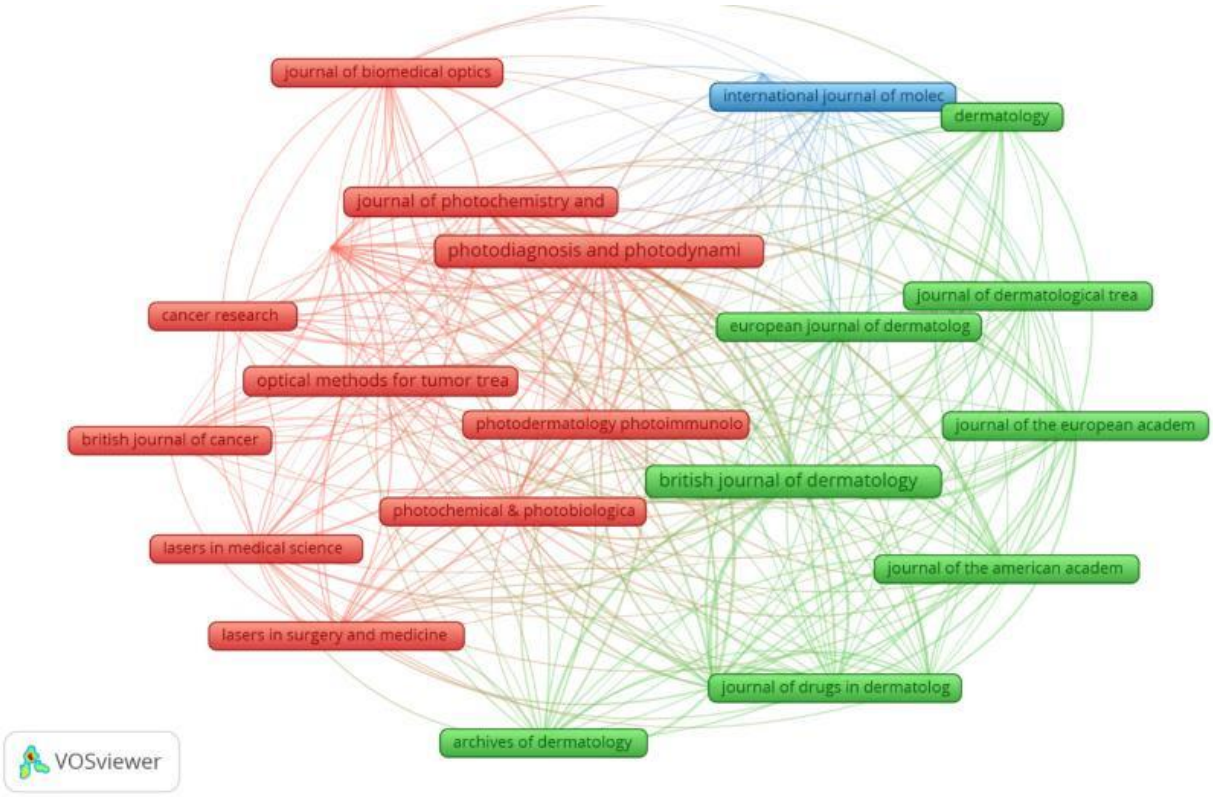

Figure 12. Bibliography Coupling of Journals.

For photodynamic treatment (PDT) research in the context of skin cancer, the Figure 13 represents a nation bibliographical coupling. With PDT, malignant cells are targeted and destroyed using light and photosensitizing chemicals. According to the production or activity of their PDT-related research, the table divides the nations into three groupings in this aspect. Brazil, Spain, Japan, and the United States are located in Cluster 1 (Red). These nations have made major contributions to PDT research on skin cancer, frequently through large-scale studies and the use of cutting-edge equipment. Germany, England, Netherlands, Denmark, Norway, and Scotland are all part of Cluster 2 (Green). These nations also produce a significant amount of research in the area, frequently working together on global initiatives and exchanging expertise. Italy, France, Belgium, Australia, Russia, and Canada make up Cluster 3 (Blue). Even though they might not be as active in PDT research as the other clusters, they are nevertheless important in improving our knowledge of skin cancer and how to treat it. The worldwide character of skin cancer PDT research and the significance of international collaboration and information exchange in this vital medical sector are show by this bibliography, which offers insights into the distribution of research activities across various nations.

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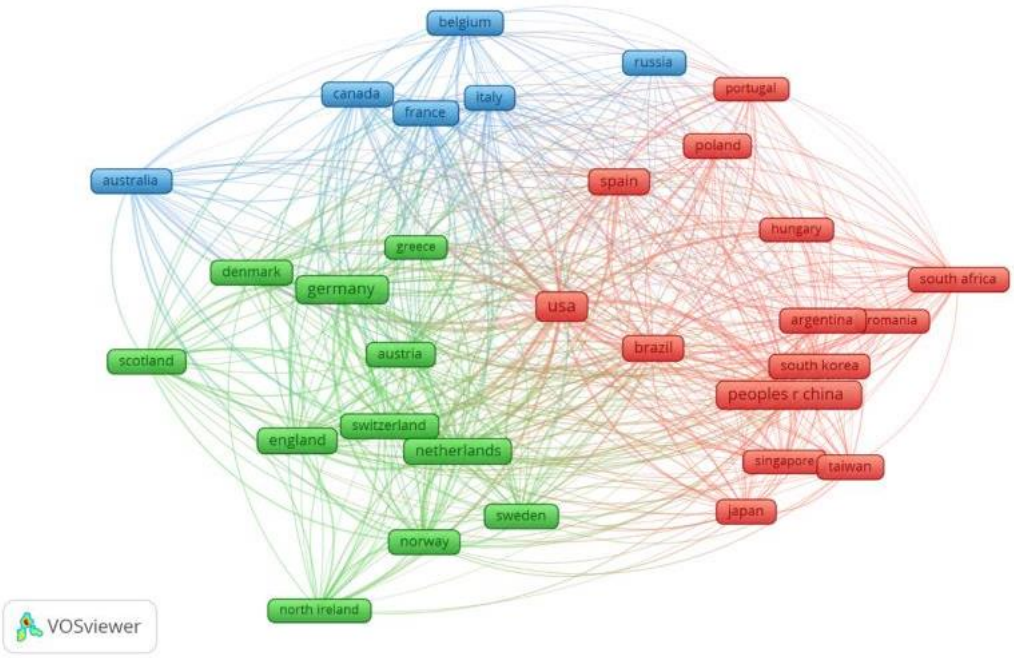

Figure 13. Bibliography Coupling of Countries

3.12 Funding Agencies

In the context of PDT research for skin cancer, Figure 14 depicts the cooperation of several funding bodies. PDT is a novel method to cancer treatment that uses light and photosensitizing chemicals to kill malignant cells. With a partnership score of 202, which indicates its substantial support and engagement in PDT research for skin cancer, the US Department of Health and Human Services is first on the list. The United States' National Institutes of Health comes in second with a score of 201, demonstrating its significant contribution to this subject. The National Natural Science Foundation of China, whose partnership score of 197 highlights China's significant involvement in PDT research, also plays a crucial role. Moreover, the National Cancer Institute of the NIH is notable due to its particular concentration on PDT applications in the therapy of skin cancer, as indicated by its score of 107. The European Union , the Spanish and the United Kingdom governments, the Conselho Nacional de Desenvolvimento Científico e Tecnológico, Fundaçao de Amparo à Pesquisa do Estado de São Paulo in Brazil, Coordenacao de Aperfeiçoamento de Pessoal de Nível Superior, and the Conselho Nacional de Desenvolvimento Científico e Tecnológico are among the other organizations actively participating in PDT research for skin cancer. This indicates the widespread interest and support for advancing this cutting-edge therapy for treatment of skin cancer.

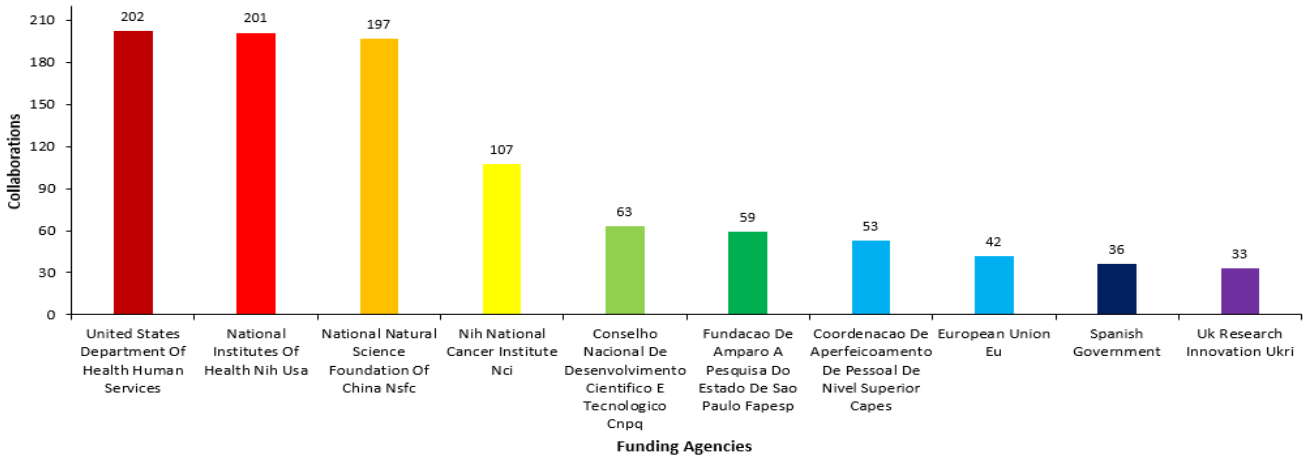

Figure 14. Funding Agencies

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3.13 Most Cited Document

Titles, publishing years, journal names, DOIs, total citations, average citations annually, and normalized total citations are only a few of the details about numerous research publications that are included in the Table 7. These publications address a variety of subjects, including dermatology, materials science, photobiology, and cancer research. The 2009 Journal of Photochemistry and Photobiology B publication by Robertson et al. has the most overall citations (837), and it stands out for having a comparatively high yearly citation rate (55.8), which suggests that the work has garnered attention over an extended period of time. With 625 total citations and a high yearly citation rate of 89.29, Van Straten's 2017 work in Cancers also stands out, demonstrating its importance in the oncology profession. Overall, based on citation metrics, the table illustrates the influence of particular works inside their respective domains and displays the variety of scientific study topics.

Table 7. Most Cited Documents.

Paper	DOI	Total Citations	TC per Year	Normalized TC
ROBERTSON CA [63], 2009, J PHOTOCH PHOTOBIO B	10.1016/j.jphotobiol.2009.04.001	837	55.8	15.32
VAN STRATEN D [64], 2017, CANCERS	10.3390/cancers9020019	625	89.29	20.27
ORMOND AB [65], 2013, MATERIALS	10.3390/ma6030817	599	54.45	15.46
TRIESSCHEIJN M [32], 2006, ONCOLOGIST	10.1634/theoncologist.11-9-1034	558	31	10.27
DAI T [66], 2009, PHOTODIAGN PHOTODYN	10.1016/j.pdpdt.2009.10.008	554	36.93	10.14
JUARRANZ A [67], 2008, CLIN TRANSL ONCOL	10.1007/s12094-008-0172-2	549	34.31	8.06
TELFER NR [68], 2008, BRIT J DERMATOL	10.1111/j.1365-2133.2008.08666.x	476	29.75	6.99
DOMINGUES B [69], 2018, IMMUNOTARGETS THER	10.2147/ITT.S134842	383	63.83	10.02
MORTON CA [70], 2008, BRIT J DERMATOL	10.1111/j.1365-2133.2008.08882.x	352	22	5.17
BRANCALEON L [71], 2002, LASER MED SCI	10.1007/s101030200027	341	15.5	5.86
ZHANG J [72], 2018, ACTA PHARM SIN B	10.1016/j.apsb.2017.09.003	337	56.17	8.82
QUE SKT [73], 2018, J AM ACAD DERMATOL-a	10.1016/j.jaad.2017.08.059	334	55.67	8.74
MORTON CA [74], 2002, BRIT J DERMATOL	10.1046/j.1365-2133.2002.04719.x	330	15	5.67
MACKAY FS [75], 2007, P NATL ACAD SCI USA	10.1073/pnas.0707742105	271	15.94	4.54
HUGGETT MT [76], 2014, BRIT J CANCER	10.1038/bjc.2014.95	250	25	8.02
PERIS K [77], 2019, EUR J CANCER	10.1016/j.ejca.2019.06.003	226	45.2	9.26
ZHEN ZP [78], 2013, ACS NANO	10.1021/nn402199g	223	20.27	5.75
NISHIYAMA N [79], 2009, ADV DRUG DELIVER REV	10.1016/j.addr.2009.01.004	221	14.73	4.05
KATO H [80], 2003, LUNG CANCER	10.1016/S0169-5002(03)00242-3	220	10.48	3.38
WANG I [81], 2001, BRIT J DERMATOL	10.1046/j.1365-2133.2001.04141.x	214	9.3	3.33
ZEINA B [82], 2001, BRIT J DERMATOL	10.1046/j.1365-2133.2001.04013.x	214	9.3	3.33
ALAM M [83], 2018, J AM ACAD DERMATOL	10.1016/j.jaad.2017.10.007	202	33.67	5.29

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HAEDERSDAL M [84], 2010, LASER SURG MED	10.1002/lsm.20860	201	14.36	5.16
BICHAKJIAN C [85], 2018, J AM ACAD DERMATOL	10.1016/j.jaad.2017.10.006	192	32	5.02

3.14 Most Frequent words

PDT is a non-invasive treatment option for a variety of skin cancers, including basal cell carcinoma and squamous cell carcinoma. This treatment applies or injects a photosensitizing chemical, often 5-ALA or a derivative, which selectively targets malignant cells while protecting healthy tissue. Once absorbed by cancer cells or precancerous lesions such as actinic keratosis, the photosensitizer is triggered by a specific wavelength of light from a light source such as a laser. This activation results in the creation of reactive oxygen species, which damage and eventually kill cancer cells. The frequency of linked phrases, with "photodynamic therapy" appearing 975 times, demonstrates the importance of PDT in skin cancer treatment as shown in Figure 15.

Furthermore, the prevalence of phrases such as "basal cell carcinoma" and "skin cancer" highlights the importance of PDT in treating these disorders. Critical components of PDT for skin cancer, such as "5-aminolevulinic acid" and its derivative and "aminolevulinic acid," are often used as photosensitizers in PDT. The name "protoporphyrin IX" refers to its essential function as an active component in the PDT process. Furthermore, "actinic keratosis" emphasizes using PDT to address early-stage skin malignancies and perhaps delay their development.

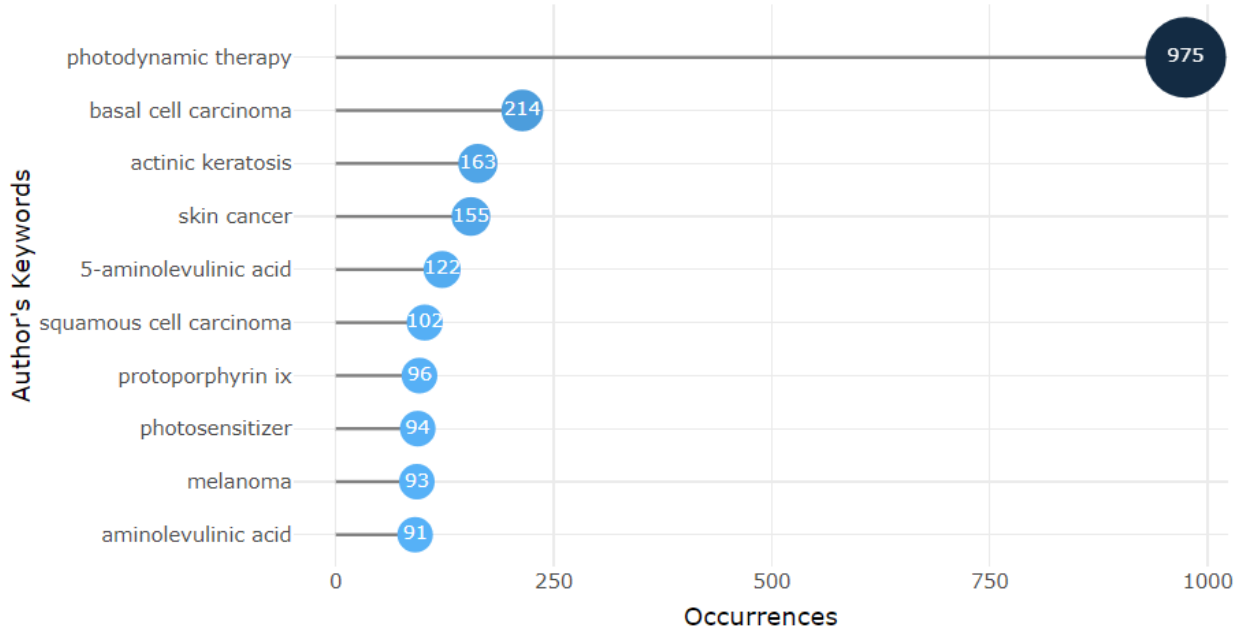

Figure 15. Most frequent words

4. DISCUSSION

Despite the intrinsic benefits of photosensitizers (PSs) in clinical use, various difficulties impede their effectiveness enhancement. The high conjugation of most PSs is a significant concern, resulting in restricted solubility or substantial aggregation in aqueous solutions. As a result, the generation of ROS in response to light activation is decreased. Furthermore, while PDT has temporal and geographical selectivity, the specificity of photosensitizers towards sick cells has to be improved because neighboring healthy cells may also absorb these photosensitizers. The sluggish clearance of photosensitizers from the body may result in ocular injury and darkening of healthy skin. To minimize adverse effects produced by residual photosensitizers, limiting light exposure following PDT for photosensitizers with significant absorption peaks in the visible light range is critical. These photosensitizer-related issues add to the general apprehension around using PDT for skin cancer and hamper future research and development efforts. The negative impact of long periods of cutaneous photosensitization and the use of 5-ALA and photofrin for treating skin malignancies [86-90]. Photodynamic treatment of HeLa cells with ALA leads to a

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significant decrease in cell viability, with approximately 90% cell necrosis observed after 18 hours of incubation with ALA and irradiation, while no decrease in cell viability is seen with ALA treatment alone [91].

To address the issues highlighted above, current efforts have focused on developing photosensitizers that successfully overcome the issues raised. Studies have been carried out to investigate phthalocyanine derivatives with high water solubility and non-aggregating qualities to increase the formation of ROS and improve their stability [41]. Furthermore, adding cell-targeting groups to photosensitizers increased selectivity while minimizing harm to healthy cells. The use of nano drug delivery systems has also gained popularity, as they provide increased biocompatibility and targeting of PSs to cancer cells, increasing therapeutic effectiveness [63]. Combining photosensitizers with oxygen-carrying groups has shown potential in combating hypoxic microenvironments during PDT. A "supramolecular" technique was also used to create intelligent photosensitizers using non-covalent intermolecular contacts, allowing for regulated photoactivity. Transition metal complexes, particularly those incorporating Ru(II) polypyridine complexes, have emerged as highly feasible PSs for PDT in skin cancer treatment. This is due to their comprehensive photochemical and photophysical capabilities, which may be efficiently used for energy and electron transfer processes. As a result, these complexes have increased photobiological activity in both oxygen-dependent and oxygen-independent pathways, allowing for more efficient PDT results [92,93].

Compared to internal organ tumors, skin cancer has distinct benefits from photosensitizers and light source irradiation. PDT outperforms established therapeutic approaches. Light-dependent photosensitizer activation in PDT allows for a more selective and accurate approach, decreasing cytotoxicity and damage to non-targeted areas, which may be unavoidable in radiation and chemotherapy. PDT is a unique feature in skin cancer that significantly decreases excessive damage to healthy tissues. Furthermore, PDT quickly and effectively eliminates all light-irradiated lesions, even possible small lesions, by leveraging the rapid generation of an abundance of ROS [64,65,94]. This method dramatically minimizes the probability of recurrence from undetected minor lesions. Additionally, hyperplastic tissue in skin cancer accumulates larger quantities of photosensitizers, displaying a unique brick-red fluorescence when exposed to UV light. This visualization assists in detecting the borders of malignant tissue and facilitates treatment planning. Third, unlike traditional surgical techniques, PDT causes minimal bleeding during treatment. This method maintains natural tissues while causing less damage. Post-treatment care following PDT requires only minor dressing changes and precise measures for light protection, improving patient ease and compliance. Furthermore, PDT exhibits low initiation or drug resistance concerns when numerous treatments are necessary for skin cancer. Furthermore, PDT can be used as a stand-alone treatment or combined with other modalities, such as radiation, chemotherapy, surgery, and gene therapy, without dynamic or immunological approaches [95,96].

Despite its benefits, numerous restrictions must be overcome before PDT may be widely used in clinical treatment. Light absorption, transmission, scattering, and reflection properties vary because of changes in skin regions, types, or coloring. As a result, different individuals or distinct regions within the same patient may respond differently to PDT, necessitating a high level of skill and experience on the part of dermatologists [97,98]. In the context of PDT for skin cancer, it is critical to address the depth of light penetration in the skin, which is restricted by light's wave-particle duality. Longer wavelengths of light can enter the skin but have less energy. However, when the wavelength surpasses 850 nm, it cannot adequately activate photosensitizers, resulting in insufficient formation of ROS and rendering it therapeutically worthless. As a result, the best wavelength range for PDT in skin cancer is 650-850 nm. Nonetheless, the light within this spectrum can only penetrate a few millimeters of skin, and as the light penetrates more profoundly, its intensity declines dramatically. As a result, PDT may be ineffective for treating profoundly invasive skin conditions [99,100-102]. Furthermore, producing ROS in PDT depends on oxygen availability. However, PDT's therapeutic efficacy is jeopardized in situations of hypoxic cancer microenvironment or deep tumor infiltration. As a result, PDT's effectiveness in treating skin cancer with deep penetration is limited. In general, ongoing research and development efforts aim to alleviate the restrictions imposed by current photosensitizers through solubility, selectivity, clearance, and adverse impact attenuation improvements. These developments can potentially improve the efficacy and safety of PDT as a skin cancer therapy [103-105].

5. CONCLUSION

Photodynamic therapy is an interdisciplinary therapeutic technique for treating skin cancer that incorporates ideas from physics, chemistry, biology, and medicine. Its non-invasive nature makes it a potential option for patients' ineligible for surgical procedures, such as the elderly, organ transplant recipients, and medically vulnerable people. PDT has shown significant success in handling difficult tumor excision in sensitive locations such as the periorbital, ocular, and paranasal regions. Furthermore, PDT provides cosmetic

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benefits while maintaining safety and efficacy. Combining PDT with additional treatment methods can improve cure rates for skin cancer cases with deep invasion or widespread coverage.

Furthermore, PDT can eliminate persistent skin cancer lesions that were too small or undetectable to detect after earlier treatments. Recent advances in PDT include the modification of photosensitizers to increase tumor cell specificity, improve the hypoxic environment, and include pro-apoptotic proteins. Exciting opportunities exist for enhancing PS skin penetration using physical techniques, such as elongated microparticles, microneedles, or derma rollers, which can improve therapeutic drug delivery. Furthermore, understanding individual features and identifying skin cancer types with low efficacy with PDT can drive attempts to improve PS effectiveness. To promote the best patient results, standardized systems for patient selection, treatment regimens, and outcome assessment in PDT for skin cancer must be established. It is crucial to highlight that PDT is not appropriate for all patients and is contraindicated in those who have porphyria, allergies to porphyrins or other photosensitizers, recent photosensitizers usage, systemic lupus erythematosus, or persistent photosensitivity dermatitis. Long-term monitoring is required to evaluate the impact of PDT on skin cancer, prevent recurrence, and monitor for metastasis.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Ethical statement

Ethical approval was nor required since this is a review study.

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