

Review

Bibliometric analysis of the use of calcium alginate for wound dressing applications: A review



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ABSTRACT

Wounds can cause many disorders and affect the quality of health, so it is necessary to develop wound dressings that have a role in accelerating the healing process. Wound dressings have evolved over time, and today there are many types of wound dressings that can suit the type of wound the patient has. This review discusses the development, types, and research directions of wound dressings from calcium alginate (CaAlg), using bibliometric analysis with time intervals from 1982 to 2021. It was found that, in the late 1990s, research related to this matter began to increase. United Kingdom, United States, China, Japan, and Italy are the five most influential countries. And from the results of the keyword analysis, it was found that, in addition to studying the general properties of wound dressings, currently there are many developments related to the structure of the material as well as the effect of adding drugs to wound dressings, so that the current study also displays various characterizations.

1. Introduction

Wounds are damage to the skin or certain tissues caused by external factors (such as injury, burns, exposure to chemicals or medical procedures: surgery) and internal factors (such as disease: impaired blood supply). Based on these factors, the wound can be in the form of incisions, tears, and bruises. Wounds can activate a variety of physiological responses. Based on the healing process, the wound is divided into two: if the reaction can contribute to wound repair without interference, it is called an “acute wound” but if the wound whose reaction is disturbed by a process, cannot heal due to disease (such as diabetes, ulcers, or cardiovascular disease) it is called “Chronic wounds” or “inert wounds” [1–3]. Wounds can disrupt blood flow, and changes in the concentration of body ions (such as calcium, zinc, and magnesium) affect the quality of health because of the pain they cause and become a major problem worldwide [4]. Currently, there are about 80 million surgeries every year in developed countries, leaving some wounds that need to be healed and the cost of wound care is very expensive [5].

Wound dressings have an important role in the healing process. So, it is very necessary to develop wound dressing materials that can adapt to the wound, are non-toxic, biocompatible, anti-bacterial, moisturizing, have appropriate adhesion (will not stick to the tissue when removed), and can encourage skin regeneration to accelerate wound healing and

have low cost [5,6]. In the mid-19th century, several textile fibers developed wound dressing materials that had a knit structure such as gauze or tulle but provided only passive protection that did not respond to changing wound conditions, nor could they be controlled or released sustainably to accelerate healing. Until George Winter introduced the concept of wet wound healing (wet healing method) by comparing wounds on animals, it was revealed that keeping the wound environment moist, would improve wound healing and healing compared to a dry wound environment [5,7].

Such biomaterials are widely used as artificial wound dressings, because they can interact biologically to treat, promote wound healing, and support skin development [8–10]. Which can be embedded in nanoparticle materials and combined with natural polymers (gellan gum, collagen, alginate, and hyaluronic acid, poly (ethylene oxide) (PEO), poly (ethylene glycol) (PEG), poly (vinyl alcohol) (PVA)), and hyaluronic acid (HA)) to improve its properties and functions [11,12]. Biomaterial polymers are of great interest in the development of three-dimensional tissues for tissue regeneration applications [13].

According to William and David, 2018 in Fig. 1. The structure and properties of a material depend on how the process and the basic materials are made, which will affect its performance [14]. So, in developing a material product, one of the points that need to be considered is the selection of the material.

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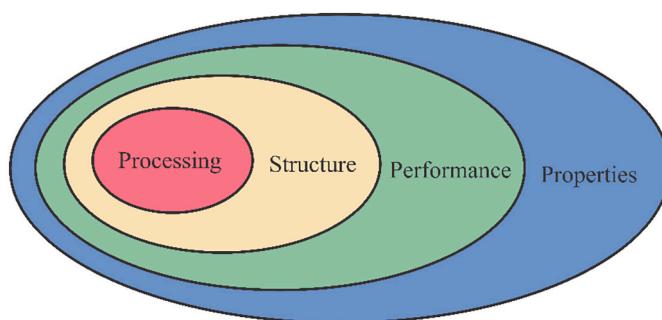


Fig. 1. The four components of the discipline of materials science and engineering and their interrelationship with the core is processing which will affect to the structure continues to the performance and finally to the properties.

Alginate is a natural polysaccharide produced by brown algae and bacteria, widely used in the food and medical industries. In recent years, alginate dressings have been developed to provide low-cost impact in treating moderate to high exudate wounds [15], as well as excellent biocompatibility, and have been in use for almost 40 years. This material is a poorly soluble polysaccharide [5,16]. Na⁺ ions in the alginate macromolecular chain can be replaced by divalent cations (i.e., Ca²⁺, Cu²⁺, and Zn²⁺). Then the macromolecular chain residues are chelated with divalent cations which will form new alginate-based polymers [17].

The diabetic wound healing was reported in ref. [18] by used cross-linking network such as polyphenol/polysaccharide hydrogel with tannic acid micro-size particles (TAMP) and guar gum (CG) as a matrix to protect the cells from oxidative damage. The Ref [19] was reported copper/tannic acid nanosheets cross-linked with sodium alginate, gelatin, and Ca²⁺ and Ref. [20] used tannic acid (TA) with quaternized chitosan (QCS) as a matrix for injectable hydrogel dressing diabetic wound healing.

The calcium cross-linked alginate is the most used material for wound care. Calcium alginate (CaAlg) dressing is an ideal filler, which is easy to fold and apply. It can also produce a gel with a high absorption capacity so that it has a very good water absorption ability, which can absorb 20 times the volume of water compared to its volume and 5 to 7 times more than traditional gauze. It can help in the healing process because some authors report that the presence of calcium ions can accelerate ion exchange in the hemostatic phase. So, it is widely used as a postoperative wound dressing. Absorption of exudate can keep the wound surface clean while maintaining a moist healing condition, which promotes the wound healing process [5,16–22].

Currently, wound dressings have been developed with different methods and basic materials and in this journal, we will discuss this with a focus on materials made from calcium alginate (C₁₂H₁₄CaO₁₂). Based on the bibliometric method that uses quantitative data as well as statistical analysis, this reviews the types of wound dressings and provides information about the direction of research on the development of research related to wound dressings made from calcium alginate. By using trend analysis of publication output, the country performance, and research hotspots and tendencies.

2. Wound healing process

The wound healing process is a complex mechanism involving a series of interrelated and overlapping steps, namely: hemostasis, inflammation, proliferation, and remodeling that lead to the repair of injured skin tissue [23]. The overall duration of the wound healing process depends on the patient's age and health status (interrupting factors such as diabetes or venous insufficiency), as well as external factors such as the presence of foreign bodies or infection in the wound.

The wound environment that is not closed and exposed to air will dry up faster, and the epithelial cells at the edges of the wound will move downwards until moist conditions are achieved which allows for cell proliferation and migration so that scar tissue will form which will delay healing. So that the use of wound dressings aims to moisturize the wound environment to accelerate healing [24]. The choice of material in the wound dressing affects the immunostimulant activity, so the wound healing phase determines the type of wound dressing that will be used for proper wound management [25,26].

The hemostatic phase (Fig. 2.a) occurs immediately after injury and this phase occurs rapidly to support rapid recovery [24]. The blood vessels that are ruptured due to the wound will become narrow and the blood flow will be stopped by platelet aggregation to form a clot of fibrin threads, also helping the coagulation of the exudate so that it will stop the bleeding that occurs [24,27].

The second phase is inflammation (Fig. 2.b). In this phase, growth factor (GF) is released locally and cell mediators mobilize inflammatory cells such as neutrophils and monocytes to the wound site. The resulting inflammatory response aims to clean the wound from foreign objects, and bacteria so that the damaged endogenous tissue will provide a suitable environment for the healing process. Injured blood vessels produce a transudate which causes swelling of the wound. The inflammatory phase is also useful for preventing infection and controlling bleeding. However, prolonged inflammation can be a problem. Hemostasis and inflammation phases occur simultaneously for 3 days [24,26].

The proliferative phase (Fig. 2.b) occurs at the end of the inflammatory phase, at this stage, the wound is completely covered by epithelial cells with the formation of granulation tissue. Where GF macrophages release fibroblasts and epithelial cells to proliferate and migrate into the wound, in this process the epithelial cells require a moist environment, this can be helped by the administration of wound dressings [28]. This phase involves the formation of new connective tissue namely vascular tissue and granulation tissue (formed by epithelial cells, fibroblasts, and keratinocytes) at the site of injury to replace dead cells as well as to replace the original clot formation. As the wound contracts, the granulation tissue is then converted into a more stable extracellular matrix (ECM). In this phase, collagen cells are also formed, which are released immediately after the formation of fibrin threads [24], in addition, there are several types of cytokines and growth factors (GF) that participate, such as the transforming growth factor-β family (TGF-β, including TGF-β3, TGF-β1, and TGF-β2), angiogenesis factors, and the interleukin (IL) family. This phase usually lasts for days or weeks [26].

The final step of the wound healing process is the remodeling phase (Fig. 2.c), in which the collagen fibers completely cover the wound surface as a new layer of skin. Collagen fibers have high tensile strength and are remodeled by crosslinking to close the wound with a strong fusion of cells at the wound edges. The tensile strength of the wound will continue to increase with collagen maturation [29]. In this phase, apoptosis also occurs where cells that are involved in wound repair but are no longer useful are removed. This phase is very fragile, this significant phase can last for months or even years. The inability of the wound to progress to this stage results in the wound becoming chronic [26].

It has been explained previously that wound dressings can play a role in accelerating wound healing, this review also discussed wound dressings made of calcium alginate, several authors reported that the presence of calcium ions can accelerate ion exchange in the hemostatic phase, this can occur because calcium ions in the dressing interact with sodium. The wound blood plasma produces wound exudate which can form fibroblasts and epithelial cells, can also modulate the proliferation and migration of epithelial cells to accelerate the homeostasis phase. Calcium alginate dressings are designed for moderate to severe exudative wounds because they have a cushion and are not made of woven or fibrous dressings so they suit the needs of the wound and have excellent vertical wicking properties [30]. Calcium alginate dressings play an

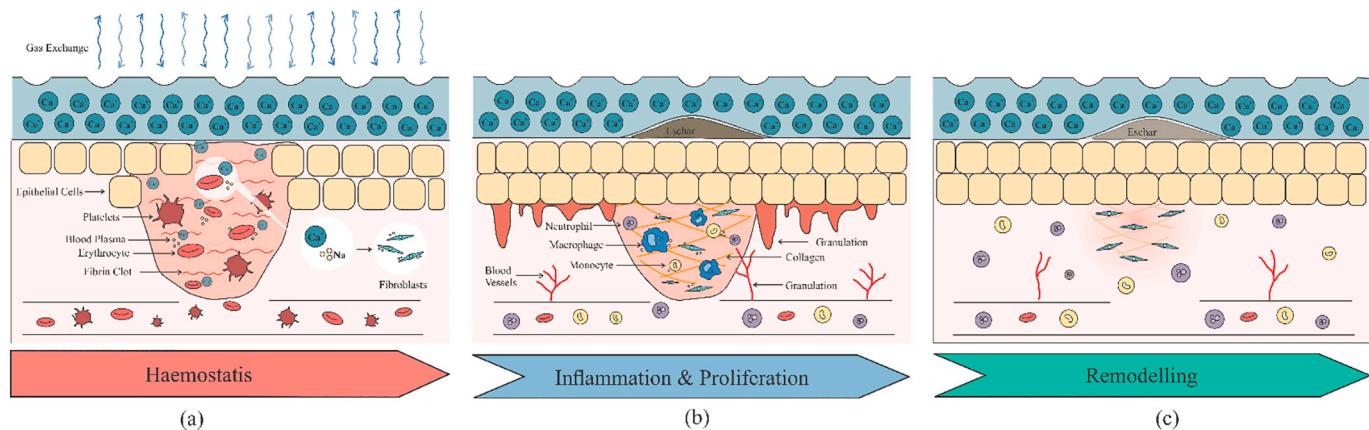


Fig. 2. Mechanism of Wound Healing (a) hemostatic phase, (b) inflammation and proliferation phase, (c) remodeling phase

active role in the granulation phase of wound healing, if the wound has granulation tissue defects and does not have a moderate amount of exudate, the dressing should be moistened with saline before use, depending on the amount of exudate, can be changed every 3 to 7 days [31], in addition to Having a high absorption capacity, calcium alginate dressings also have anti-bacterial properties and good wound management, so they can protect the wound from infection [32].

3. The Bibliometric methodology

Bibliometrics is a comprehensive technology that uses statistical analysis to describe the distribution of quantitative changes and the relationship between each document, where the search results can be exported to software for further analysis such as VOSviewer [31], so that it can be used to analyze developments, identify weaknesses, strengths, and weaknesses. and research gaps and can reveal research trends in various research fields [34,35].

It was invented by Professor Chaomei Chen of Drexel University in early 2004 to make statistical visualization analyzes of scientific references, and is characterized by a co-citation network map of cited references, cited authors, and cited journals, as well as a word map co-occurrence network, keys, terms, authors, and so on [36]. This method has two parts, namely bibliometric analysis of performance, and analysis of science mapping to know various characteristics attached to publications, such as periodic information of publications, publication productivity, cooperative publication modes of various countries, the geographical distribution of publications, and keywords at various stages, publications [33,37].

4. Method

4.1. Data source

Literacy review in this journal, using the Scopus database as a data source. Journal information about wound dressings made from calcium alginate, was extracted using search keywords, namely TS = (wound dressing) AND TS = (calcium alginate). The year of publication of the first document related to research is used as the starting point until the last year for this bibliometric analysis, namely 1982–2021 (a span of 39 years) and a total of 585 documents were obtained. The search was limited to the publication of only English-language documents and excluded other types of documents other than articles, reviews, and conference papers, and a final total of 475 documents was obtained.

4.2. Data analysis

In analyzing bibliometric data, this journal uses openrefine software

(3.6.1). To visualize data, Professor Chen Chaomei developed scientific visualization software based on the assumption that scientific knowledge changes. In visualizing bibliometric data, this journal uses Vosviewer (1.6.18) and Tableau software (Fig. 3).

5. Result and discussion

5.1. Bibliometric analysis of publication output

Fig. 4 shows the temporal development of three types of documents (articles, reviews, and conference papers) based on the number of documents published each year and the number of document citations each year related to research on calcium alginate wound dressings, where the x-axis shows the annual development from 1982 to 2021., the left side of the y-axis represents the number of documents issued each year and the right-hand side of the y-axis represents the number of document citations each year. Of the number of documents obtained, articles accounted for 363 documents (80.67 % of the total document), reviews had 68 documents (with a percentage of 15.33 %) and the least was conference paper, which was only 18 documents (4.00 %) as shown in Table 1.

As shown in the figure, the number of published documents reached a peak of 34 documents (in 2020) for article documents, 7 documents (in 2004 and 2013), and for conference papers, there was not too much increase, this can be seen in the number of most of the documents only have 2 documents (in 2000, 2004, 2011 and 2013). It can also be seen, that the number of published documents shows a gradually increasing trend, Wound dressings using the wet method were widely developed during the 1980s so that the increase in the number of research publications was only about $\pm 1\text{--}5$ documents each year, then over the next two decades many have been published. Proving the benefits of this can be seen in the increase in the number of published documents reaching ± 10 document articles every year and continues to increase in proportion to the increasing number of needs as well [38]. This indicates that related research topics are increasingly interesting and it is also important to continue to develop them.

In addition to the development of the number of document publications, we also reviewed the increase in the number of cited documents. The quantity value is further explained in Table 2. We divide the development into three parts so that each part is analyzed every 12 years. In the table, the document types that contributed the most documents were articles, then reviews, and finally conference papers, with a total of 221, 101, and 41 documents for each range. However, if you look at the average percentage of citations for each document, the review ranks first with the number in each range, namely 94.11 %, 96.96 % and 100 %. The possibility of this happening is because the paper review displays a lot of comparisons between each topic discussion, such as a

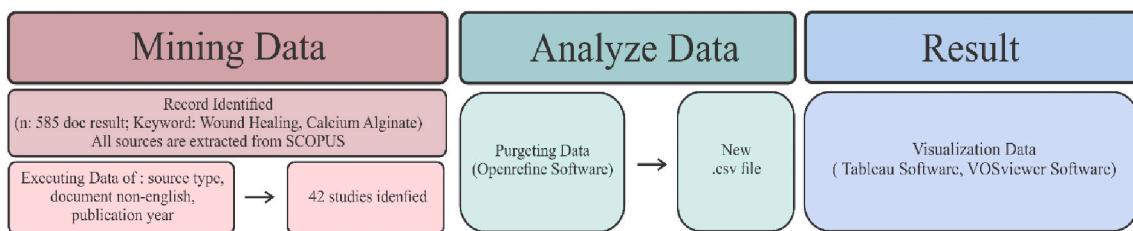


Fig. 3. Bibliometric analysis mechanism

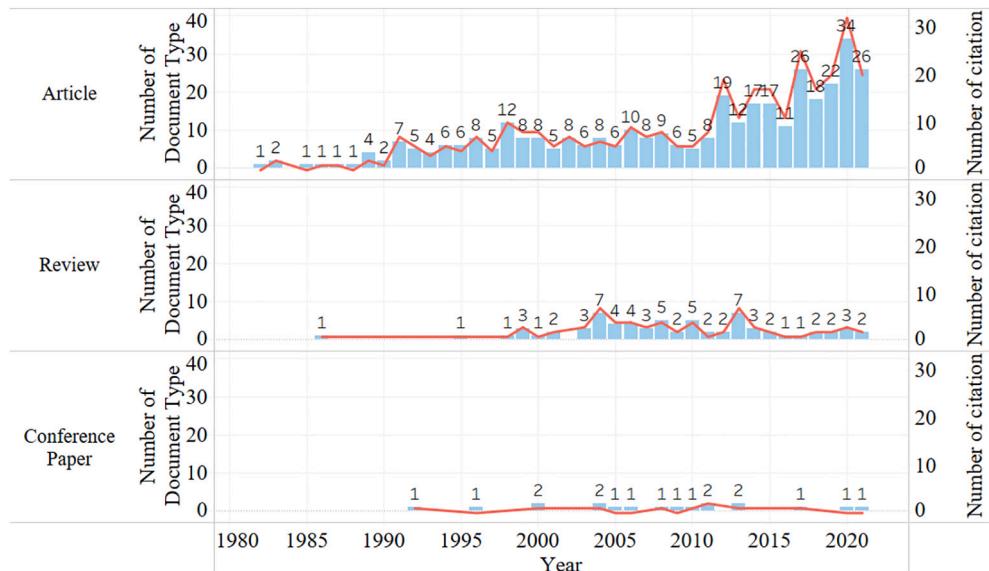


Fig. 4. Number of cited and Number of all publications (articles, conference papers, reviews) on wound dressing by calcium alginate.

Table 1
The trend of document publication.

Range pub. (year)	Document type	Total document	Total cited	Percentage of citations per paper (rank)
Range I (2009–2021)	Article	221	207	93.66 % (2)
	Review	33	32	94.11 % (1)
	Conference Paper	9	5	55.55 % (3)
Range II (1996–2008)	Article	101	89	88.11 % (2)
	Review	33	32	96.96 % (1)
	Conference Paper	8	3	37.50 % (3)
Range III (1982–1995)	Article	41	31	75.60 % (3)
	Review	2	2	100 % (1)
	Conference Paper	1	1	100 % (2)

comparison of the types of methods used, materials used, and types of wound dressings. so that it is often cited as a reference for research to be developed. The percentage of >90 % displayed also conveys that almost all publications from document reviews have been cited.

5.2. Bibliometric analysis of the citations

5.2.1. Source publisher and publisher analysis

It was found that from all published documents, there were 287 types

of source publishers. Fig. 5 describes the 15 types of source publishers who are most active in related research, which are grouped based on the number of published documents and the number of citations used, the average publication owned by a source publisher has 4–17 published documents. Journal of wound care occupies the top position which contributes the most published documents (as many as 17 documents), then followed by the international journal of biological macromolecules (as many as 16 documents) and wound UK (as many as 9 documents).

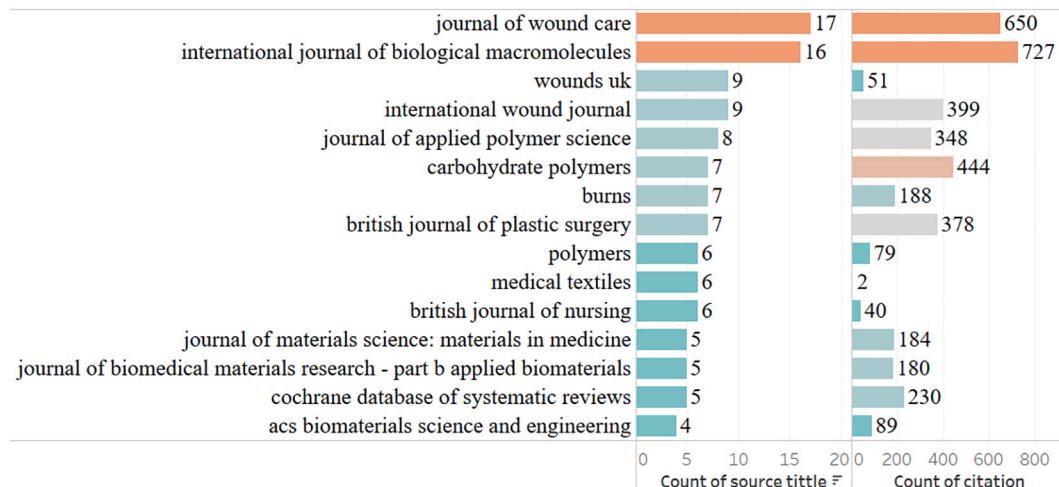
Table 2 shows developments related to research based on 7 indicators, namely: number of published documents and cited documents, year of publication, h-index, total link strength of source publishers as well as their relationship with publishers, sorted by number of published documents. It has been explained previously that the Journal of wound care occupies the first position based on the number of documents published, but based on the number of citation documents, the International Journal of Biological Macromolecules has a larger number, namely 727 citations (number of citations per document: 45.43 times), and the Journal of Wounds. care occupies the second position having 650 citations (number of documented citations: 38.23 times). and for the British Journal of Plastic Surgery, although it only has 7 documents and the number of citations is 378, it is superior in the number of citations per document, which is 54 citations in each published document. In addition, the h-index is a way that can be used to measure the broad impact and relevance of scientific findings [39], so we also analyze the source publishers that have a large impact based on their h-index, and the Cochrane Database of Systematic Reviews ranks first with a total h-index of 292.

We also analyze the relationship between source publishers, which is visualized using the Vos Viewer and shown in Fig. 6, where each circle represents the source publisher, and cooperation and the size of the

Table 2

Journals with the highest number of documents published for wound dressings made from calcium alginate.

Rank	Sources Publication	Publisher	Country	H-Index	Coverage's year	Number of documents	Number of citations	Number of citations per paper	Total link strength
1	Journal of Wound Care	Ma Healthcare	United Kingdom	68	1995–2021	17	650	38.23	37
2	International Journal of Biological Macromolecules	Elsevier	Netherlands	144	1979–2021	16	727	45.43	26
3	International Wound Journal	Wiley-Blackwell Publishing	United Kingdom	70	2004–2021	9	399	44.33	21
4	Wounds UK	Wounds UK	United Kingdom	20	2006–2021	9	51	5.66	9
5	Journal Of Applied Polymer Science	John Wiley & Sons Inc.	United State	175	1959–2022	8	348	43.50	27
6	British Journal of Plastic Surgery	Oxford University Press	United Kingdom	210	1913–2021	7	378	54	27
7	Burns	Elsevier	United Kingdom	108	1974–2021	7	188	26.85	15
8	Carbohydrate Polymers	Elsevier	United Kingdom	228	1981–2022	7	444	63.42	25
9	British Journal of Nursing	Ma Healthcare	United Kingdom	50	1992–2021	6	40	6.66	2
10	Medical Textiles	International Newsletters	United Kingdom	3	1984–2008	6	2	0.33	0
11	Polymers	MDPI AG	Switzerland	89	1969, 2009–2021	6	79	13.16	6
12	Cochrane Database of Systematic Reviews	John Wiley And Sons	United Kingdom	292	1998–2021	5	230	46	9
13	Journal Of Biomedical Materials Research - Part B Applied Biomaterials	John Wiley & Sons Inc.	United state	116	2003–2021	5	180	36	3
14	Journal Of Materials Science: Materials in Medicine	Springer Netherlands	Netherlands	133	1990–2021	5	184	36.8	18
15	ACS Biomaterials Science and Engineering	American Chemical Society	United State	62	2015–2021	4	89	22.25	7

**Fig. 5.** The top 15 most active source publishers by the count of documents and citation.

circle are obtained from the number of citations, it can be proven that the International Journal of Biological Macromolecules has the largest circle, for the lines connecting these circles represent their cooperation [40], and the number of lines and their thickness illustrates the strength of the collaboration [41] and it can be seen that the Journal of Wound Care has a line of work At the same time the most (37 total link strength) there are also source publishers who do not have cooperation, namely Medical Textiles with a total link strength of 0, both of which can be seen in Fig. 6a.

Meanwhile, Fig. 6b shows a visualization of its development based on its year distribution, and the color in the circle adjusts the year of publication [40]. The yellow color is for the 2020 interval, and the dark

blue color is for the 2000-time interval. In Fig. 6b. the early development of this type of wound dressing is evidenced by the color of the source publisher Medical Textiles (1984–2008) is dark blue, where textile is a material composed of fibers so that it is included in wound dressings with the dry method. Then the material used began to develop using a wet method that uses polymer-based materials, this is marked by the color of the source publisher Carbohydrate Polymers (1981–2022) is green and the source publisher Polymers (1969, 2009–2022) is yellow. In addition, the International Journal of Biological Macromolecules (1979–2021) also has a yellow color, this can happen because based on the scimago, the journal in it contains the latest research and the novelty of previous research so this source publisher is still developing until now

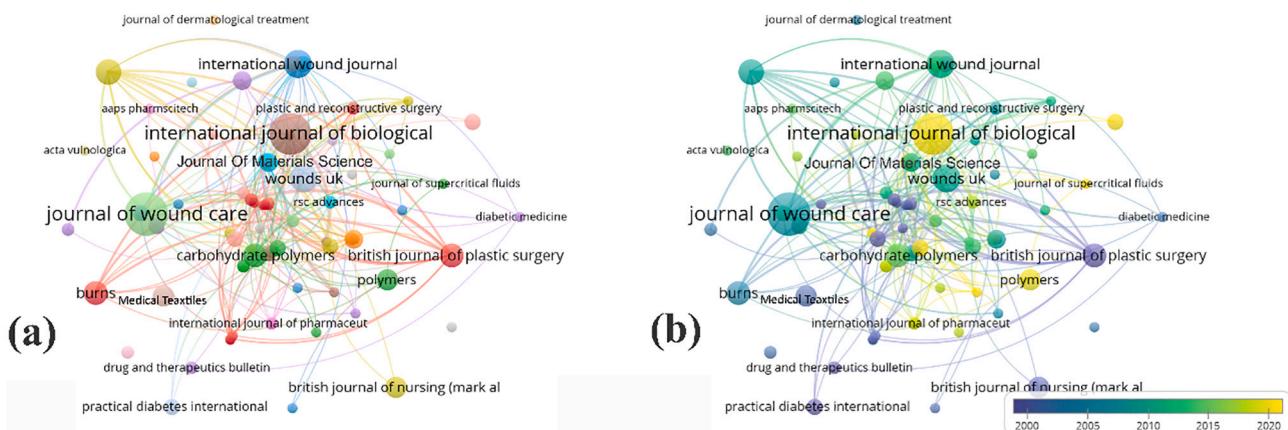


Fig. 6. The citation of source publisher (a) collaboration network, (b) Trend by the year (from 1982 to 2021).

and its scope includes biological activities and interactions, molecular associations, chemical and biological modifications, and functional properties.

Then, in the publisher analysis, all documents that have been collected are published in 99 types of publishers, Fig. 7 is the top five publishers based on the total documents owned. Elsevier is the publisher that contributed the most to literacy, with 47 documents, the second being MDPI AG (13 documents), followed by John Wiley and sons (10 documents), American chemical society (8 documents), and Lippincott Williams and Wilkins. (8 documents). This can also be seen in Table 2, which is from the top 15 source publishers based on the number of documents, Elsevier appears to appear 3 times.

Table 2 also provides information about the country of origin of the source publications, and the United Kingdom appears 9 times and is the country that appears often. Then the second position was filled by the United States which appeared 3 times, then there was the Netherlands which appeared 2 times, and the last time it appeared 1 time.

5.2.2. Source affiliation analysis

The top 10 productive affiliations related to research on wound dressings made from calcium alginate sorted by the number of cited documents are shown in Table 3. University of Greenwich (457 times) with the publication of document review (1), then there is the University of Miami (400 times) with the publication of document articles (1) and others. Overall, the top earning affiliates come from the United Kingdom which shows the country's activeness in contributing to research-related publications, followed by the United States and Portugal. Also compared to article (4), review (6) is the type of document that is highly cited by the affiliate.

5.2.3. Bibliometric analysis of the author

Table 4 provides data on the contributions of citation 5 authors based

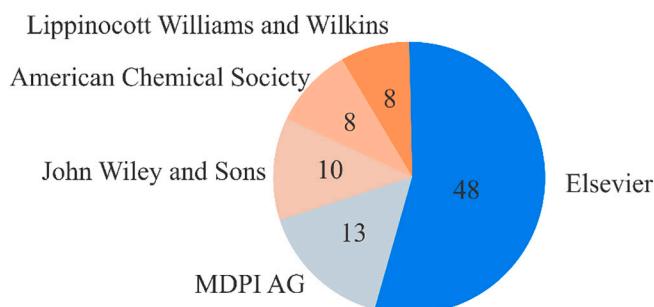


Fig. 7. The top 5 publisher-based numbers of the total document.

Table 3

Top 10 productive affiliations of wound dressing by calcium alginate research.

Rank	Affiliations	Country	Document Type (n)	The number of citations (n)
1	University of Greenwich	United Kingdom	Review (1)	457
2	University of Miami	United State	Article (1)	400
3	Universidade do Porto	Portugal	Review (1)	338
4	University of Fort Hare	South Africa	Review (1)	288
5	Jiaxing College	China	Review	265
6	National University Hospital	Singapore	Article (1)	249
7	University of Coimbra	Portugal	Article (1)	245
8	Imperial College School of Medicine	United Kingdom	Review (1)	244
9	Johnson & Johnson Wound Management	United States	Article (1)	224
10	Princess of Wales Hospital	United Kingdom	Review (1)	214

on the total document citations they have and their visualization is shown in Fig. 8. Qin Y, from China (Jiaxing College: especially in the Biochemical Materials Research and Development Center), is the researcher who has contributed the most to research on sanitary napkins. CaAlg wound with a total citation of 510 times with the number of documents: Article (3) and Review (2), this can happen because in his journal there are many things he discusses CaAlg wound dressings, namely: the production process, comparisons between types of additional materials (such as Zn, Silver, Sodium, etc.), the comparison between the types of seaweed as the base material for alginate, the comparison of the material composition, and the structure of the wound dressing (polymer and fiber), which are used as a reference for various analyses: absorption qualities, ion exchange processes, and also their application to wounds.

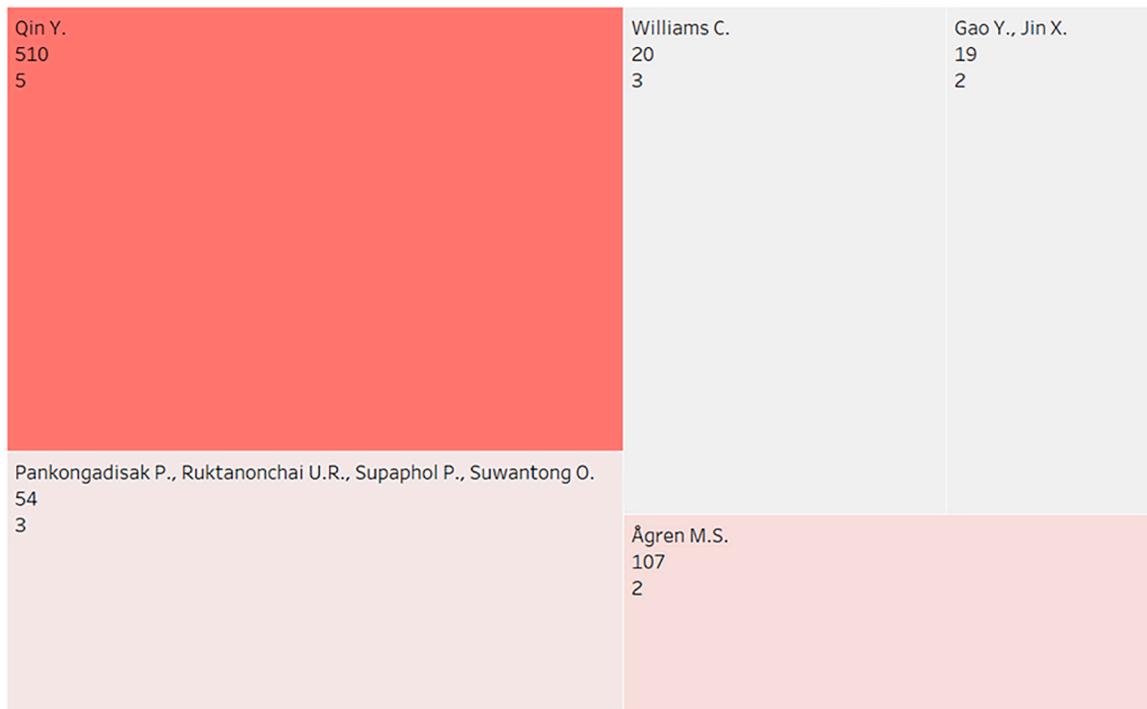
The second author who has had an impact on related research for the second place is gren M.S., originally from Denmark (particularly from the pathology department) who had 107 citations and contributed an article (2). In general, his research conducted in vitro tests on domestic pigs using hydrogel with an amorphous structure to improve the physical properties of hydrogel wound dressings and compared 4 different types of CaAlg wound dressings.

Then there are Pankongadisak P, Ruktanonchai U.R, Supaphol P, and Suwantong O, although they come from different agencies but come from the same area, namely Thailand. Has a total of 54 citations with the number of publications Article (2). Research conducted quite rarely, namely developing wound dressings made of CaAlg beads using the electrospray method by analyzing the concentration of Alginate and

Table 4

Top 5 authors' contribution to wound dressing by calcium alginate research.

Authors	Countries	Document Type (n)	Document's year	Number of citations (n)	Ref
Qin Y.	China	Article (3)	2004, 2006	510	[42–46]
Ågren M.S.	Denmark	Review (2)	2008	107	[47,48]
Pankongadisak P., Ruktanonchai U.R., Supaphol P., Suwantong O.	Thailand	Article (2)	1996, 1998	107	[49–51]
Williams C.	United Kingdom	Article (3)	2014, 2015, 2017	54	[15,52,53]
Gao Y., Jin X.	China	Article (2)	1994, 1998, 1999	20	[54,55]
			2018, 2019	19	

**Fig. 8.** The top 5 authors' contributions by total citation.

stress on the shape and diameter of the sample.

Followed by Williams C, from the United Kingdom (specifically: Wrexham Maelor Hospital), having a total of 20 citations with a total document: Article (3). The research focused on several types of CaAlg wound dressings: Algosteril, Melgosorb, and Kaltostat.

The last one is Gao Y and Jin X from China with a total of 19 citations, from the article (2) related to CaAlg fiber wound dressings made with a pore structure, discussing their effect on wound exudate absorption, ion exchange, and degradation behavior of wound dressings based on: degradation process, degradation mechanism, and variations in the performance of degraded dressings and their effect on wound healing.

5.3. Bibliometric analysis of country performance

5.3.1. Contribution of different countries

based on the number of publications of the green document, the country is visualized in Fig. 9, if the more color documents are closer to 1 and the pinker the total document is 89. the total number of countries that contribute to research related to CaAlg injury is 61. The 10 most active countries based on published documents and the number of citations is shown in the form of bars in Fig. 10.

The ranking of countries based on their total document citations is shown in Table 5, the United Kingdom (3316) occupies the first position, it is known that wound dressings have a very important role in the healing process and chronic wound care in the United States, almost 20 billion dollars in annual costs., this is what makes the United States

active in developing research related to wound dressings. Then followed by the United States (3086), which spent 184 million pounds on the use of wound dressings, and in the global market, it is estimated that 2019 will reach a value of \$20.4 billion in 2021 from \$17.0 billion in 2016 [5]. Because it is constrained by funding and lack of availability, giving reasons that the development of research related to wound dressings is urgent to do. Then the active countries are China (1464), Japan (757), Italy (643), and so on.

5.3.2. International collaboration patterns

International cooperation between countries can be seen in Fig. 11. The four countries with the most citations have a close relationship, namely the United Kingdom, the United States, China, and Japan. And the country that has the most cooperative relationships is the United Kingdom, this can be seen in the lines connected to the United Kingdom and by looking at the total link strength value in Table 5.

5.4. Research hotspots and tendencies

5.4.1. Article keywords analysis

The keywords are used in the entire collected document; the network map is visualized using VOSviewer in Fig. 12. The minimum keyword occurrence is set for 5 times out of 4529 total keywords, only 543 keywords are found that meet the analysis. Each circle represents a keyword. The bigger the circle, the higher the appearance. The distance between keywords shows the relationship, the shorter the distance, the

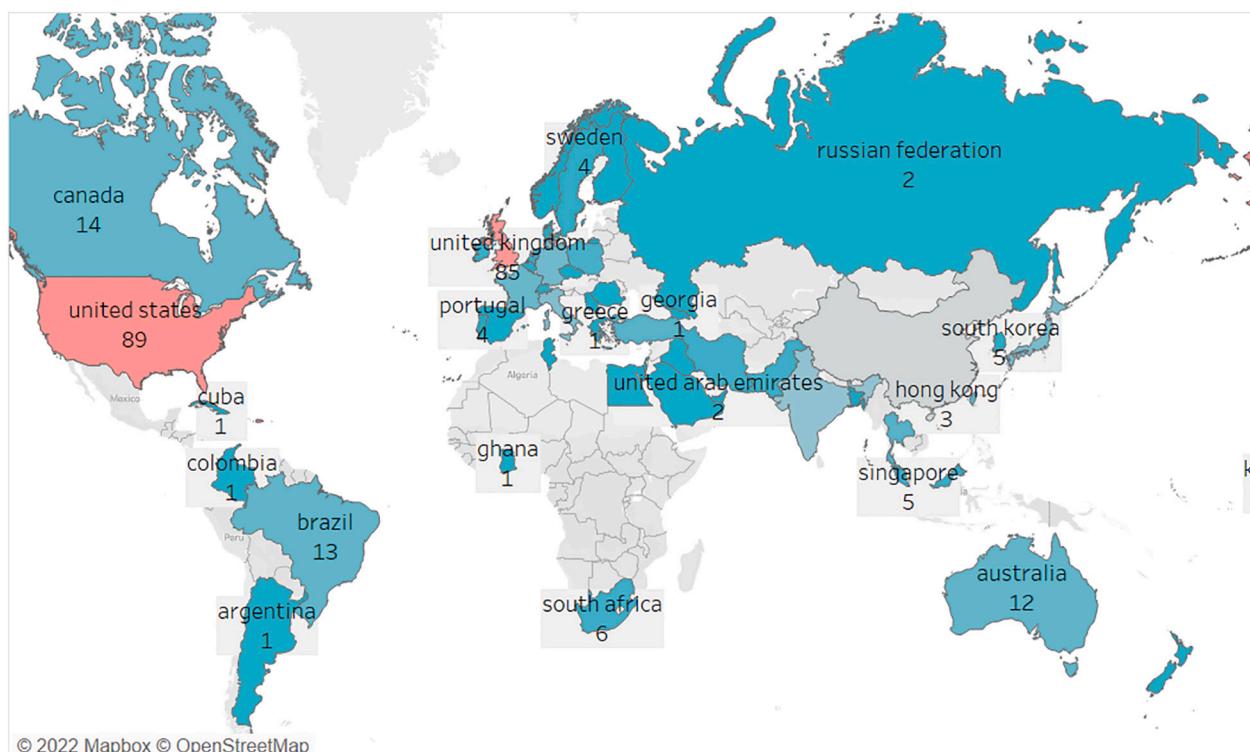


Fig. 9. The geographical location of contributing countries.

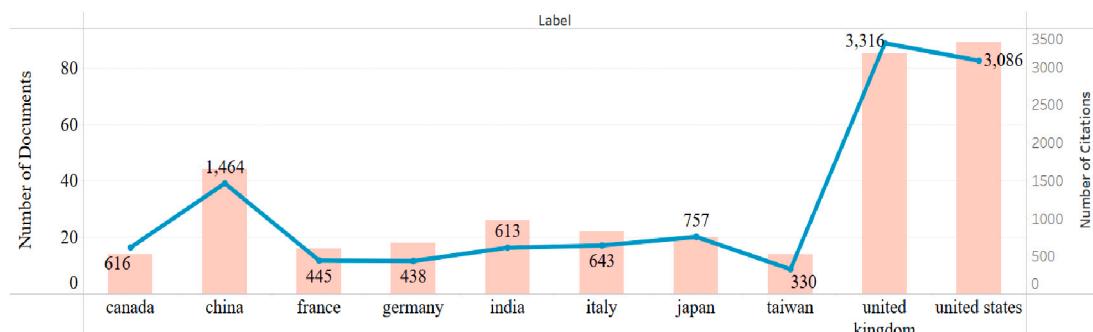


Fig. 10. Number of documents and citations from top 10 contribution countries.

Table 5
Top 10 most productive countries based on citation counts.

Rank	Country	Number of documents published (n)	Number of citation counts (n)	Total link strength
1	United Kingdom	85	3316	226
2	United States	89	3086	114
3	China	14	1464	122
4	Japan	20	757	58
5	Italy	22	643	52
6	Canada	26	616	9
7	India	18	613	36
8	France	16	445	25
9	Germany	44	438	33
10	Taiwan	14	330	30

stronger the correlation between keywords [39]. The color in the circle reflects the relationship between keywords that are adjacent and are in the same cluster [41].

Analysis of keywords is divided into 3 different cluster colors: cluster I (red: 251 items), Cluster II (green: 216 items), and cluster III (blue: 74 items), this cluster division can reflect the type of literature discussed related to wound research. CaAlg dressings. Cluster I consist of 4 main keywords: Calcium Alginate, wound dressing, wound healing, and humans. This explains the effect of CaAlg wound dressing on wound healing in humans, which shows that the lines in the four circles have a short distance and have a close relationship, it is also seen that the branching discusses a lot of factors that can affect wound healing in humans such as age, type of wound, and method of wound care.

This is to the research that has been done, in which wound healing is a complex biological and molecular event (involving various cells), and the wound healing process depends on several factors, namely the level and depth of skin damage, type of wound, infection, and age [56,57].

Cluster II discusses more things that can support the performance of wound dressings on non-humans. The main keywords are hydrogel (a type of wound dressing), non-human, anti-infective agent, antibacterial activity, biocompatibility, absorption, and drug delivery system, which were tested using the in vitro study method so that there are several characterizations such as Fourier-transform infrared spectroscopy.

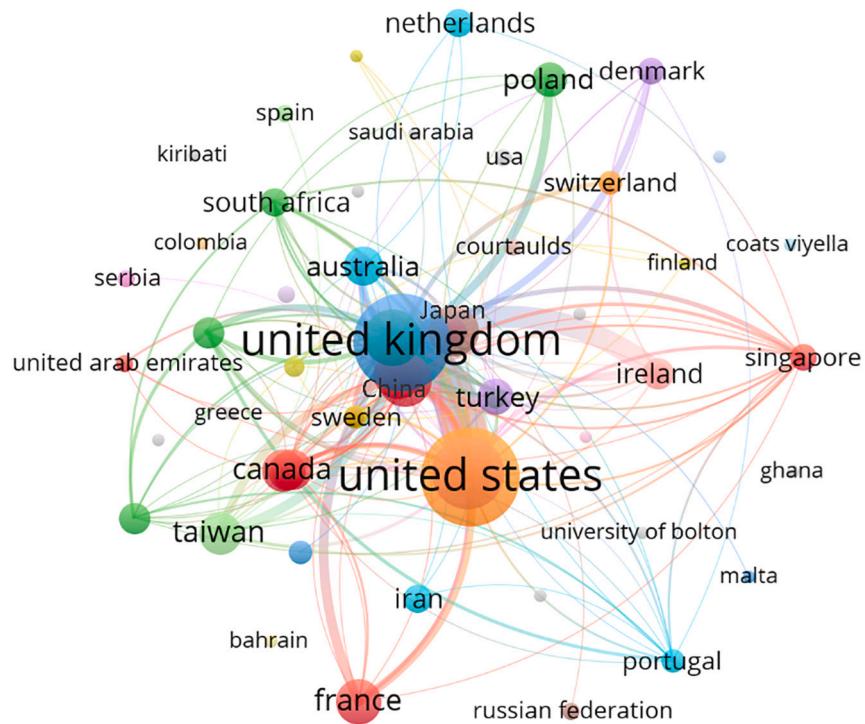


Fig. 11. Cooperation between countries.

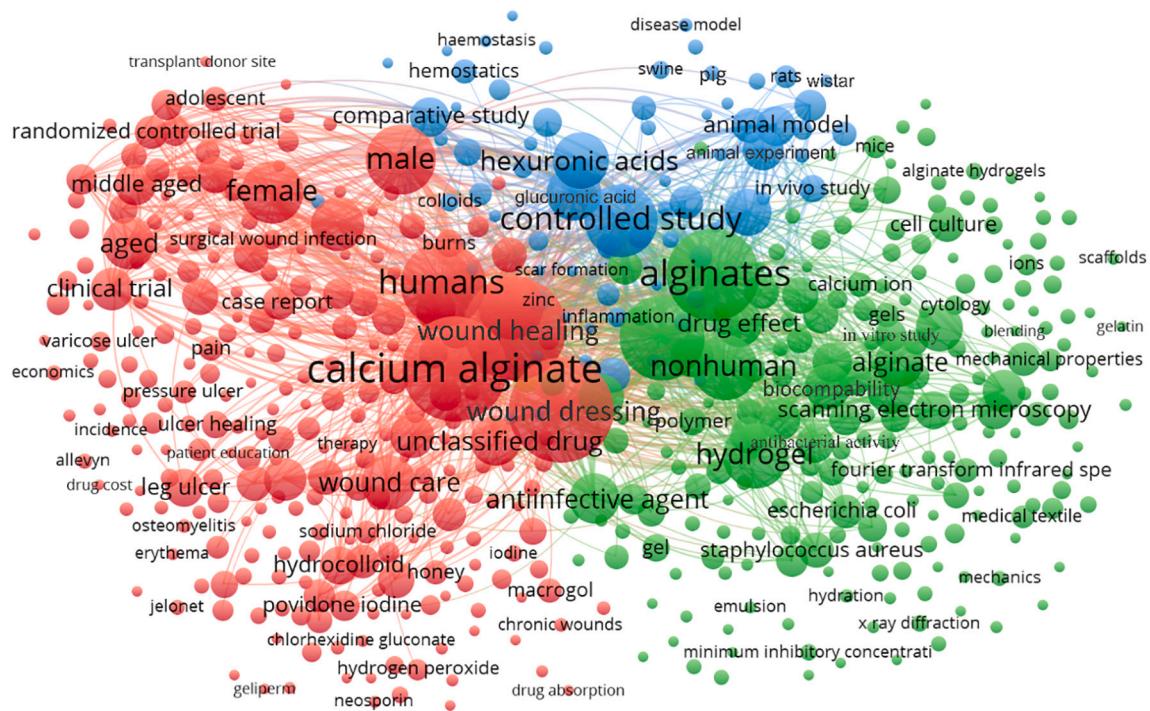


Fig. 12. Co-occurrence network of keywords.

(FTIR), scanning electron microscope (SEM), X-ray diffraction (XRD).

In Cluster III, the main keywords are controlled study and comparative study, so the type of literature in this cluster discusses a lot of research that compares the presence of one or more in different samples or at different times. Like doing testing on pigs, rats, mice, and Wistar.

5.4.2. A Brief history of wound dressing

The concept of keeping wounds clean and dressing wounds has long been known, one of which is found in clay tablets found in Mesopotamia (2200–2500 BC), which describe the 3 points of the healing movement: washing wounds, making plasters, and dressing wounds. In ancient times, people used a mixture of natural materials such as mud or clay as well as herbs [58,59].

The Egyptians (1400 BC) were probably the first to use bandages, they used honey (as an anti-bacterial), oil (as an anti-infective, because bacteria grow badly there, also preventing the bandage from sticking to the wound), and fiber (as a barrier and aids drainage). Wounds (usually made of vegetable fibers: leaves and grass), it is also done to remove dead skin and pus to promote wound healing. People also think that the art of wrapping corpses in balm in Egypt was done to prevent decay [58].

Then Hippocrates who was a Greek (400 BC), emphasized the importance of cleanliness in wounds that were washed using wool that had been boiled in water or wine or vinegar (acetic acid) first. It is also believed that wounds heal faster if allowed to remain dry [60]. In ancient times, World War I and II resulted in many being injured, thus making people learn a lot about wound healing. And in the fifth century BC wound dressings were widely used.

In the 18th century, the science of wound surgery developed, and for the first time, the Johnson and Johnson company (1891) mass-produced surgical dressings by sterilizing cotton and gauze, as well as antiseptic dressings [59].

Wound dressings with the dry method continued to develop until the 19th century, starting to apply wound dressings with the wet method which was first introduced by Winter (1962) [7]. The types of wound dressings are shown in Fig. 13. Generally, traditional wound dressings (dry method) are used for clean, dry wounds with light exudate levels.

So, at the end of the 20th-century people began to develop modern wound dressing products with the wet method, which has better absorption properties than traditional dressings, but keeps the wound moist [38] (Fig. 14).

The development of the type of wound dressing with the wet method was analyzed from the use of keywords in the document and visualized using VOSviewer. Where yellow is the type that is currently being developed, and dark blue illustrates the opposite. And explain the

characteristics of the wet method of wound dressings, it is shown in Table 6. Which, the total occurrence describes the number of attendances in all documents.

Based on Table 6, it was found that hydrogel wound dressings have elastic properties that can avoid injury when removed, and usually have a transparent structure, so they are easy to control without being removed. It can also form a moist environment in the wound which is suitable for use on dehydrated wounds. Hydrocolloid wound dressings consist of two layers, consisting of an outer layer of waterproof material and an inner layer consisting of a hydrogel pad based on an inner colloid layer that adheres to the skin. Having an opaque morphology makes it difficult to monitor the wound but is suitable for wounds with heavy exudative. For foam wound dressings, consist of two layers: an outer semi-occlusive layer, and an inner layer consisting of foam and having a porous structure that can support cell infiltration. Also suitable for high exudative wounds. And for film wound dressings, semipermeable, thin, transparent, and elastic materials are also ideal as drug carriers. However, due to its poor absorbing properties, it can only be used on low exudative wounds.

5.4.3. Themes and trend topics analysis

In addition to learning about the properties of good wound dressings, in recent years, releasing some drugs or antibiotics in dressings has been shown to inhibit bacterial growth [75], also paying attention to the mechanical properties that lead to an elastic or flexible texture that can follow the patient's movements, and must also have good tensile strength because the wound dressing should not be damaged while in use, so that it can affect the healing process [76,77].

The current research on wound dressings is not only focused on the general properties that wound dressings should have but has begun to pay attention to the development of the material structure [78] and drug release in the dressing [79], so many studies have started using many

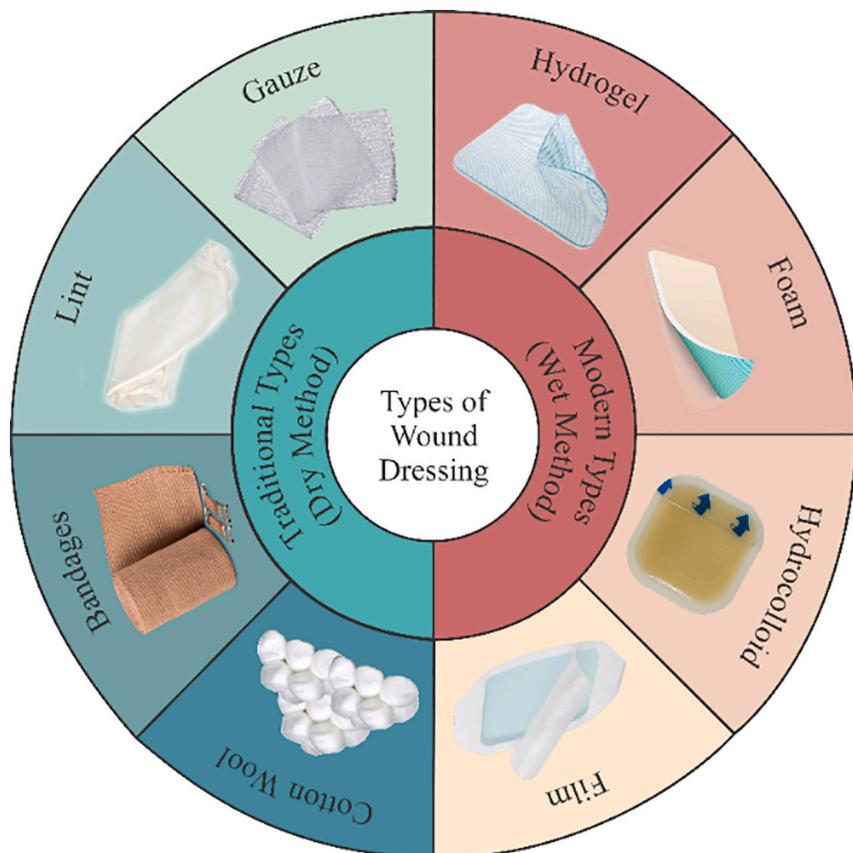


Fig. 13. Types of wound dressing.

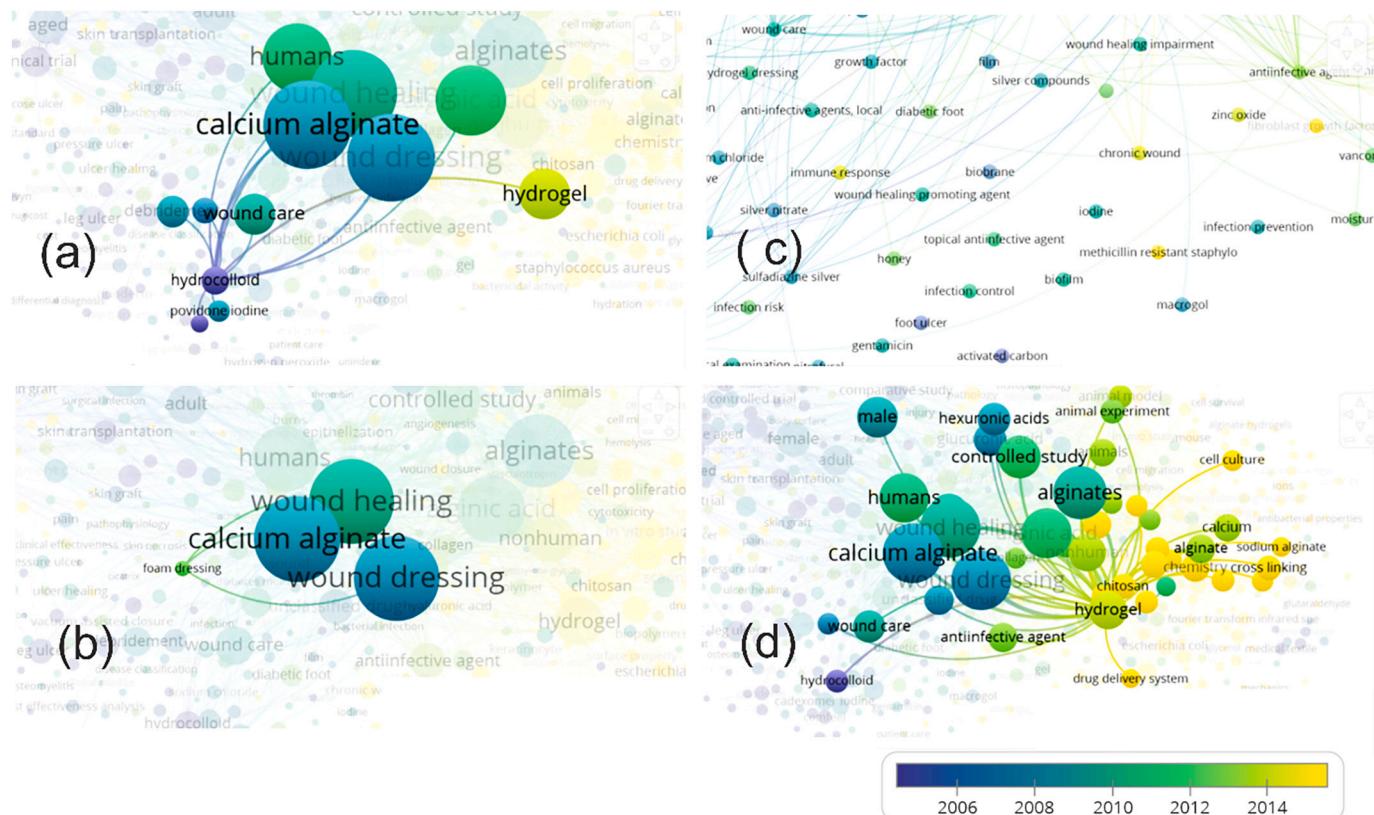


Fig. 14. Analysis of the trends of the type of wound dressing by calcium alginate by keywords network.

variations of characterization such as XRD, FTIR, SEM, TGA, etc., to test the mechanical pads which will certainly affect their performance, this is also in line with the visualization shown in Fig. 15 which is the distribution of the use of keywords based on time. The yellow color describes the types of keywords that are currently used frequently.

Several studies have shown that studies on sample characterization can affect the performance of wound dressings, such as using SEM (Scanning Electron Microscopy) analysis to describe the structure of the dressing, where samples with porosity can affect their absorption capacity, and pore sizes with microporous and mesoporous scales have the power excellent or good absorption than macro size, due to high specific surface area and high pore volume also allows the exchange of gases and nutrients needed by cells [78,80]. FTIR analysis (Fourier-transform infrared spectroscopy) was used to see the functional groups formed to test the efficacy of the cross-linked method of incorporating the drug into the wound dressing [78,81]. TGA (Thermogravimetric) analysis was used to test its thermal stability [82]. And, XRD (X-Ray Diffraction) analysis is usually used to see the structure of the wound dressing (amorphous or crystalline) [78,83].

6. Conclusion, challenges, and future direction

This study discusses the history, development, and research trends related to Calcium Alginate wound dressing, using the bibliometric method by analyzing: the trends of publication output, the citations, Country Performance, and Research hotspots and tendencies. By extracting data from the Scopus database as many as 475 documents with an interval of 1982–2021. Based on the number of documents analyzed, the increase every year, it was found that research related to wound dressings began to increase in the late 1990s since the discovery of wet dressings. From the analysis of publishers, affiliates, and authors, it is found that 3 countries are actively contributing related: the United Kingdom, the United States, China, Japan, and Italy. Where the United

Kingdom has the highest number of document citations, and the United States has the highest number of documents.

From the keyword analysis, it describes a general discussion of related documents discussing the effect of calcium alginate wound dressing on wound healing, and it is also found that review journals have a lot of influence on comparative studies of several variables (can be seen in the number of citation documents). The analysis of keywords based on the time distribution can describe research trends related to CaAlg wound dressings. In addition to studying the general properties of wound dressings, there are currently many developments related to the structure of the material as well, so the current study also displays various characterizations.

For future research first, should be focus for the effect of additional drugs to wound dressings on wound-healing processes. The second, find the potentials sources of natural alginate from the agricultural waste, seaweed, and weed plant which may present sustainable and protect the environment. The third, possible and continue research for development new and natural calcium alginate as a wound dressing including selection natural biomaterials, economical synthesis, and production process, and increase biosorption and purity of calcium alginate To increase wound healing ability, the material should be used cross-linking materials from natural resources to press the production of reactive oxygen species (ROS) which can induces oxidative damage to the biomolecules. The most important parameter for wound healing is physical properties such as elasticity and mechanical properties, how the drug delivery to the wound by molecular interaction, and surface biofunctionalization for more effective and efficient at the specific wound such as diabetic.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Table 6

Summary of wound dressing types by wet method.

No	Type of dressing	Description	Characteristics	Caution	Clinical Applications	Commercially Available Product	Total link strength	Total Article (occurrence)	Usage Time (days)	Ref
1	Hydrogel	are soft elastic properties and wet materials with a large amount of water in as three-dimensional (3D) hydrophilic networks and usually clear or transparent	✓ easy application removal after the wound was healed without any damage monitoring of the wound without removing the dressing. ✓ keeping the wound moist ✓ capable of absorbing large quantities of water or biological fluids without dissolving. ✓ adhesion-free coverage of sensitive underlying tissue ✓ pain reduction through cooling	✗ May overhydrate wound (can cause maceration) ✗ need secondary dressings for protection ✗ Caution in infected wounds	✓ dry chronic wounds ✓ Pressure ulcers, ✓ skin tears, ✓ surgical wounds, ✓ burns, ✓ radiation oncology	CellerateRX® (Wound Care Innovations LLC), Regenecare® Wound Gel (MPM Medical Inc.), Wun'Dres® (Coloplast AG),	113	2830	1–3	[24] [61] [62] [63]
2	Hydrocolloid	semi-permeable material that are consist of two layers: outer waterproof, does not need a secondary dressing which adheres to the skin. Are available as sheets, pastes, and powders.	✓ easy to use, can reduce external friction and shear, has self-adhesive, waterproof, does not cause the pH of the wound surface to drop; the acidic environment can inhibit bacteria growth ✓ Excellent exudate absorption properties	✗ difficult to the monitoring of the wound without removing the dressing ✗ are occlusive so that they can cause maceration of the skin around the wound due to excessive moisture ✗ not recommended for use in diabetic foot ulceration, very highly exudative wound, necrotic and infected wound	✓ decubitus ulcers ✓ Severe exudative wound ✓ ideal for abrasions, post-operative wounds, pressure ulcers, ✓ shallow ulcers on the legs	DuodermE® (Convatec), Bristol Myers Squibb, France) Algoplaque®HP (Urgo, France) Algiste®M calcium alginate (Kaltostat®) Comfeel®Plus Coloplast Nexcare™	43	1151	2–4	[61] [64] [65] [66] [67]
3	Foam	consists of two layers: the outer layer is semi-occlusive, and the inner is composed of hydrophilic (water-absorbing) polyurethane foam and has a porous structure.	✓ Designed to absorb wound exudate while maintaining a moist wound surface ✓ effective absorption of wound exudate ✓ Because of its porous structure, it can improve the osteogenic differentiation of gas exchange. ✓ High porosity and interconnectivity foams are supporting cell infiltration.	✗ need secondary dressing for protection ✗ It is difficult to visualize wounds without removing the dress because it is opaque. ✗ burr-shaped so it is necessary to remove the pads to control ✗ not recommended for wounds covered with necrotic (so it can stimulate excessive granulation	✓ very comfortable over bony prominences ✓ for wounds to severe exudative ✓ Wounds with sensitive epithelial cell surface	Allevyn (Smith & Nephew), Biatain (Coloplast) Tegaderm (3 M)	23	620	daily to once or twice weekly	[24] [61] [68] [69] [70] [71]
4	Film	Are polyurethane sheet with an adhesive coating to the side, is semipermeable, thermal insulation has thin, transparent, and elastic (It is easy to	✓ comfortable for the patient to wear, ideal drug carriers, low cost. ✓ easy to control without having to remove the pads ✓ can reduce pain and the possibility of	✗ May strip skin upon removal ✗ Do not use on infected or strong exudative wounds (film can trap liquid and cause maceration)	✓ dry wound: low exudative ✓ small abrasions ✓ first degree burns ✓ Preventing skin damage,	Blisterfilm™ (The Kendall Co) Carrafil™ (Carrington Laboratories) Mepore Film (Molnlycke Health Care)	12	382	a few times weekly	[5] [61] [72] [73] [74]

(continued on next page)

Table 6 (*continued*)

No	Type of dressing	Description	Characteristics	Caution	Clinical Applications	Commercially Available Product	Total link strength	Total Article (occurrence)	Usage Time (days)	Ref
		adapt to complex forms and angles of wounds).	trauma to the wound, facilitate the process of mobility and maintain patient hygiene ✓ permeable to gases (water vapor, oxygen, and carbon dioxide) but not permeable to bacteria and liquid water (exudates) due to its semi-occlusive nature.		phase 1 pressure ulcer	Opsite™ (Smith & Nephew)				

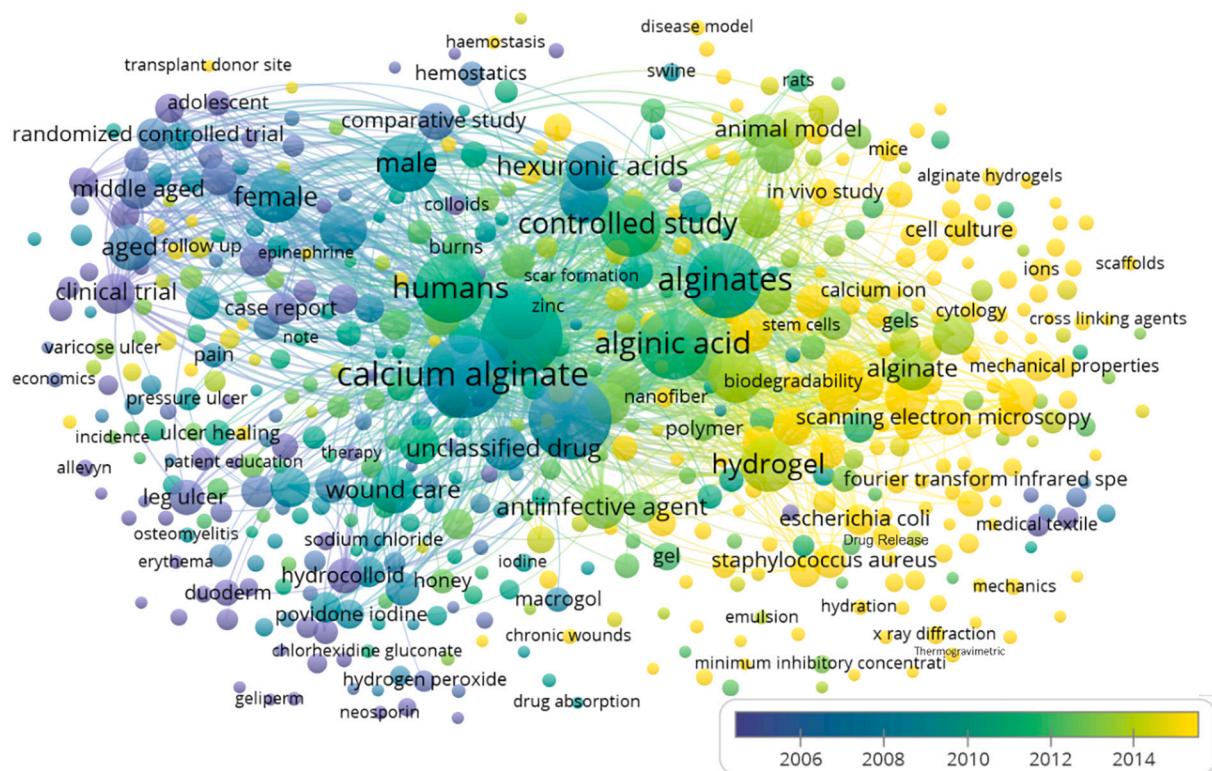


Fig. 15. Trend topic-based Keywords evolution network.

Data availability

Data will be made available on request.

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