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RESEARCH ARTICLE

A Bibliometric approach for Analyzing the Potential Essential Oil Microemulsions

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ABSTRACT:

Essential oils are bioactive compounds consisting of various pharmacological or therapeutic activities capable of causing changes in color and odor with unstable characteristics. Several studies have been conducted to overcome these problems by developing essential oil into microemulsion dosage forms. However, none have been conducted to identify the trends and patterns quantitatively through a collection of research publication documents. Therefore, this study identified the developments and areas of focus on essential oil microemulsions using bibliometric methods. Data was collected from PubMed from 2000 to 2021 and analyzed using R-studio and VOSviewer software. The results showed that 2020 had the largest number of publications, with 114 documents widely published in China. The most productive author, Oknologi S, used the keywords "Essential oils" and "microemulsions" 47 and 21 times, respectively. The trend of publications related to essential oil microemulsions is expected to increase with its continuous development.

KEYWORDS: Bibliometric, Microemulsion, Essential oil.

INTRODUCTION:

Essential oils in pant are complex volatile mixture exist at low concentrations and are commonly found in aromatic plant[1]. The role of essential oils in pharmacological, therapeutic, and cosmetic activities is popular. Essential oils act as antibacterial[2], anti-inflammatory[3], anticancer[4], antifungal[5], and antiviral[6] substances. According to Xavier-Junior et al. (2017), essential oils are also used as biocides against various microorganisms such as bacteria, fungi, viruses, insects, and plants. These substances contain bioactive compounds in terpenes such as limonene, menthol, carvone, and thymol. They can be used for good skin penetration with low systemic toxicity due to the high levels of phenolics and antioxidant activity[7].

Shabrina et al. (2020) stated that essential oils have unstable characteristics because they can undergo oxidation, polymerization, and resinification due to heat and sunlight. Oxidation reactions can also cause changes in color and odor[8]. Therefore, these oils need to be formulated in a more stable preparation form, such as developing a drug delivery system known as microemulsions. These thermodynamically stable systems are clear, transparent, and have high solubility[9,10].

The development of research in the field of essential oil microemulsions can be known by conducting bibliometric analysis. Bibliometric analysis of scientific publications related to research themes is an important component of microemulsions[11]. This method can quantitatively identify research trends and patterns through a collection of documents. It also provides a systematic and reproducible review process capable of evaluating an overall picture of a research area[12]. The advantage of the bibliometric method is that it can assess the quality and evaluate the development of a specific topic by comparing results between agencies, documenting changes, and predicting potential research by identifying its focus areas[13].

There are many studies that have been carried out on bibliometric analysis, including bibliometric analysis in chemical research and chemical engineering, material

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research, covid-19 research, magnetite nanoparticles, and research on the production of nanocrystalline cellulose. However, research has not been carried out specifically to determine the development of research on bibliometric analysis of published data in the field of essential oil microemulsions. Based on the background, this research conducts a bibliometric analysis of scientific publications on essential oil microemulsions from 2000 to 2021. It is expected to be a source of literacy to develop research on essential oil formulations.

MATERIALS AND METHODS:

Data were collected from https://pubmed.ncbi.nlm.nih.gov because it consists of 22 million citations for biomedical literature from MEDLINE, life science journals, and online books. Literature searches were conducted using the PubMed search engine with the terms microemulsions and essential oils. The articles were taken from 2000 to 2021 to determine the number of publications, distribution by country, journals, authors and publications, collaboration with co-authorship, and frequency of keywords.

The data obtained were then analyzed using R studio and VOSviewer software. R studio software was used to analyze the number of publications each year, the distribution of articles per country, institution, and journal, as well as the author's name and the number of publications. Meanwhile, VOSviewer software was used to visualize data and analyze co-authorship based on the authors' name, institution, co-occurrence, and keywords.

RESULT:

Trends in the number of published articles each year:

This research used 119 published articles stored in PubMed from 2000 to 2021. The number of articles fluctuated yearly, with the highest number of 18 obtained in 2020 and the least, 1 in 2000, 2004, 2006, and 2009, as shown in (figure 1).

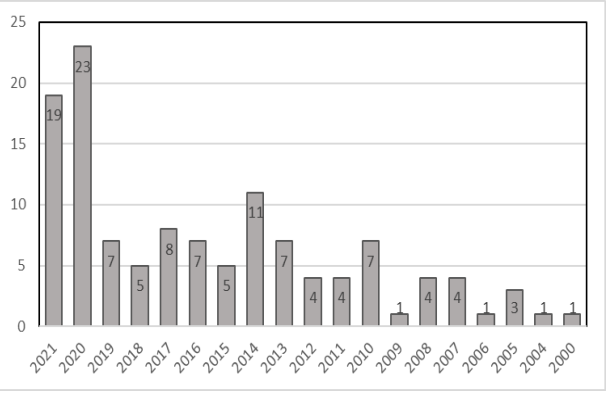

Figure 1: Number of essential oil microemulsion articles

Distribution of articles by country and institution:

Research on developing essential oils into microemulsion preparations has been carried out by 29 countries and 212 universities. (Figure 2) and (Table 1) show the 15 countries and universities that publish the most articles on essential oil microemulsions, with China topped the list with 114 (24.62%) followed by Brazil with 96 (20.73%).

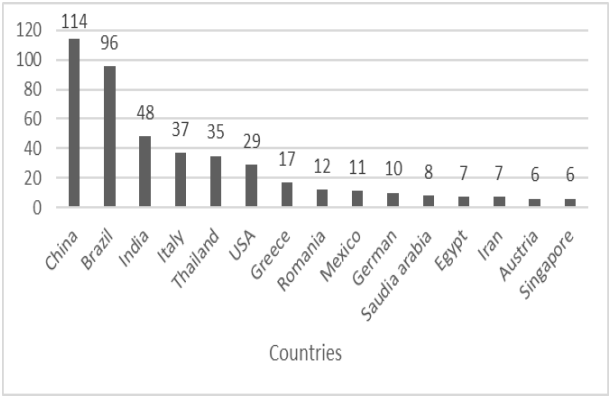

Figure 2: Distribution of articles in the most 15 countries

The three highest-ranking institutions are Chiang Mai University (Thailand), Nanjing University of Chinese Medicine (China), and the University of Michigan (United States). Although institutions from China are ranked second, their numbers with Brazil are 6 and 4, as shown in (table 1). The highest number of institutions that publish articles is also presented in ranks 1 and 2.

Table 1: Distribution of the most 15 institutions

Rank	Institution	Count	%
1	Chiang Mai University (Thailand)	35	16.13
2	Nanjing University of Chinese Medicine (China)	23	10.60
3	University of Michigan (United States of America)	12	5.53
4	School of Perfume and Aroma Technology (China)	11	5.07
5	Sao Paulo State University (Brazil)	11	5.07
6	State University of Paraiba (Brazil)	11	5.07
7	Federal University of Sergipe (Brazil)	10	4.61
8	Shoolini University of Biotechnology and Management Sciences (India)	10	4.61
9	De Montfort University (United Kingdom)	9	4.15
10	Programa De PS-Graduao Em Cincia Animal Da Universidade Federal De Gois (Brazil)	9	4.15
11	VIT University (India)	9	4.15
12	Dalian Medical University (China)	8	3.69
13	Chinese Academy of Medical Sciences And Peking Union Medical College (China)	7	16.13
14	School of Chinese Materia Medica (China)	7	16.13
15	Shaanxi University of Chinese Medicine (China)	7	16.13

Distribution of the number of articles in journals:
This bibliometric analysis shows that 105 articles have been published in 63 journals. (Table 2) indicates that the International Journal of Pharmaceutics, with 7 numbers at 11.48%, is published the most.

Table 2: Distribution of the number of articles in journals

Rank	Journal	Count	%
1	International Journal of Pharmaceutics	7	11.48
2	Food Chemistry	5	8.20
3	Journal of The Science of Food and Agriculture	5	8.20
4	Zhongguo Zhong Yao Za Zhi = Zhongguo Zhongyao Zazhi = China Journal of Chinese Materia Medica	5	8.20
5	Aaps Pharmscitech	4	6.56
6	Colloids and Surfaces. B Biointerfaces	4	6.56
7	International Journal and Food Microbiology	3	4.92
8	Langmuir: The Acs Journal of Surfaces and Colloids	3	4.92
9	Pharmaceutics	3	4.92
10	Drug Delivery and Translational Research	2	3.28
11	Drug Development and Industrial Pharmacy	2	3.28
12	Drug Discoveries & Therapeutics	2	3.28
13	Electrophoresis	2	3.28
14	International Journal of Cosmetic Science	2	3.28
15	Journal of Agricultural and Food Chemistry	2	3.28
16	Journal of Colloid and Interface Science	2	3.28
17	Journal of Food Science and Technology	2	3.28
18	Journal of Oleo Science	2	3.28
19	Molecules (Basel Switzerland)	2	3.28
20	Nanomaterials (Basel Switzerland)	2	3.28

Name of authors and number of publications:
(Table 3) indicates no dominant work by an author or researcher. Almost all of the authors have an average of 5 research publications, the most prolific being essential oil microemulsion research by Okonogi S with a total of 6.

Table 3: Number of articles by authors

Rank	Name of Authors	Number of article
1	Okonogi S	6
2	Chaiyana W	5
3	Chandrasekaran N	5
4	Edris Ae	5
5	Mukherjee A	5
6	Anuchapreeda S	4
7	Wang Y	4
8	Franklyne Js	3
9	Liu X	3
10	Wu Q	3

Collaboration of authors with co-authorship:
(Figure 3) shows the pattern of collaboration between authors, which is visualized and used to determine a minimum and maximum limit of 4 documents for each author and 25 authors per document. Based on these limitations, 4 out of 599 authors fulfill the criteria, as shown in (figure 4). The largest connection of anuchapreeda songyot and chaiyana wantida as well as okonogifinorn and time singkome were found in clusters 1 and 2. This shows a pattern of collaboration in each cluster.

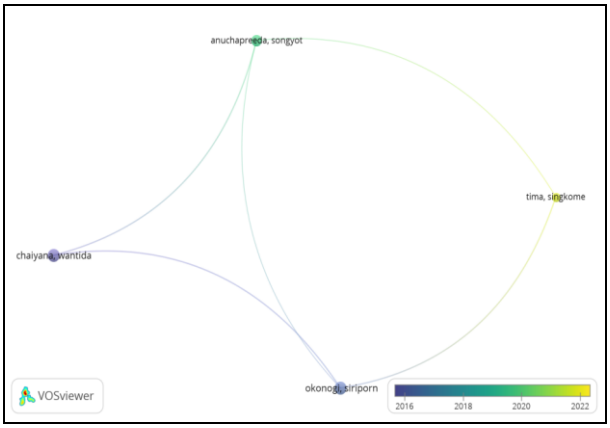

Figure 3: Pattern of collaboration between authors

The limitation of this institutional collaboration analysis is the minimum number of 2 documents. (Figure 4) shows that out of 231 institutions contributing to research related to essential oil microemulsions, 5 fulfilled this limitation. (Figure 4) shows the existence of 5 clusters without collaboration between institutions.

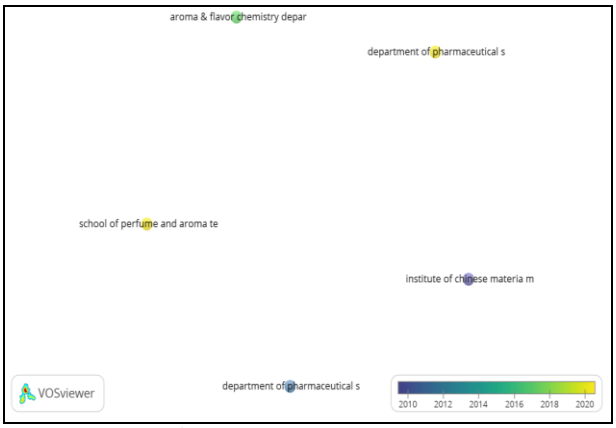

Figure 4: Pattern of collaboration between institutions

Frequency of keywords:
This research used keywords to identify the dominant knowledge structure of essential oil microemulsions. The documents used are related to author keyword frequency analysis and hierarchical map charts published in the titles and abstracts of scientific research. The co-occurrence analysis of keywords

identifies the microemulsion structure and essential oils with a domain dataset consisting of 336 documents and 15 keywords, as shown in (figure 5). Emulsions are the most widely used keyword, followed by essential oils and microemulsions at 62, 47, and 21 times, respectively.

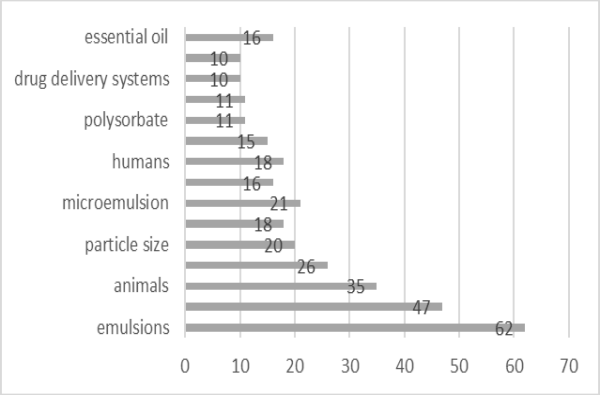

Figure 5: Number of essential oil microemulsion keywords

Keywords can summarize the articles' focus and determine certain trends from research based on its analysis. This cluster analysis is carried out based on the co-occurrence of all keywords with a minimum of 5 occurrences for each and a total of 741 used by the authors. (Figure 6) is a visualization of keywords in scientific publications from 2000 to 2021 containing the terms "microemulsions and essential oils" in the titles and abstracts found in the PubMed database and analyzed using VOSviewer with a minimum number of 5 documents. (Figure 6) shows a pattern or map of correlation between clusters describing a collection of keywords with homogeneous entities and the same attributes. Each cluster is represented with a different color. The thickness of the connecting line per keyword indicates the occurrence rate and the relationship strength of those determined based on the network's total strength.

(Figure 6) shows a total of 4 clusters, where the first is marked with a yellow color group which is research on the activity of essential oil microemulsions as antibacterial and anti-infective. The second is a purple cluster containing the essential oil microemulsions used as a drug delivery system where stability should be maintained. The essential oils are obtained from the tea plant, whose contents are analyzed using gas chromatography. The third is a blue cluster, which discusses the content of essential oils such as terpenes, acetylcholinesterase, and polyethylene glycol. Meanwhile, the fourth is a green cluster, which discusses the stability test of microemulsion preparations as a drug delivery system consisting of solubility, particle size, and viscosity.

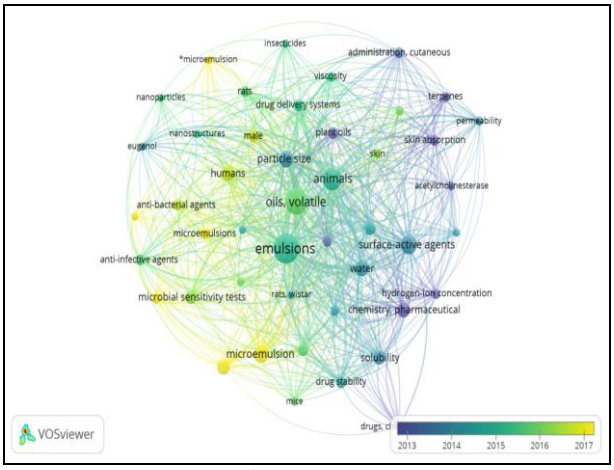

Figure 6: Visualization of keyword link overlays on scientific publications

DISCUSSION:

The biblometric method analuzed 119 article related to the essential oil microemulsion during 2000-2021. The number of articles published every year has been up and down. From these data, it can be seen that in the last 10 years research on essential oil microemulsion is still relatively rare every year. The formulation and development of novel drug delivery system with the nature of enhancing the effectiveness of existing of drug is an ongoing process in pharmaceutical research. Since there are many types of drug delivery systems that have been developed [14]. Microemulsions are currently the subject of many investigations because of their wide range of potential and actual utilizations. The high capacity of microemulsions for drugs makes them attractive formulations for pharmaceuticals. These systems also offer several benefits for oral administration, including increased absorption, improved clinical potency and decreased toxicity[15].

Most of the article were form China, and six out of fifteen at most was from China. Base on the source of the article’s funding, we speculated that the Chinese government fully supported the research in this field. The number paper originated from China for 67.75% of the total, indicating that scientist in China have contributed most of the research results on the essential oil microemulsion in the past decade.

The analysis of collaboration between authors can describe the pattern and relationship of collaboration with organizations through published documents[16]. This analysis can also be applied to assess the productivity of research, and its relationship between technological and scientific developments, map priority focus areas, and evaluate the contribution of institutions and researchers[17].

This research used keywords to identify the dominant knowledge structure of essential oil microemulsions. The emulsions keyword is widely used because microemulsion is a dispersion system developed from its preparations. In some pharmaceutical and cosmetic applications, both microemulsions and emulsions could be the dosage form of choice. Emulsions are heterogeneous system in which one immiscible liquid is dispersed as droplets in another liquid. Such a thermodynamically unstable system is kinetically stabilized by addition of one further component or mixture of components that exhibit emulsifying properties[18]. One emulsion that is further dispersed into another continuous phase is called double emulsion, multiple emulsion or emulsified emulsion[18]. Another emulsion system is "microemulsion". Microemulsions have advantage over the convention emulsion, it form upon simple mixing of the components and do not require the high-shear conditions[19]. In particular, a low energy input in the preparation is involved due to its spontaneous formation and physical stability. Many characteristics of microemulsions make these preparations to be used as a drug delivery system compared to emulsions[20].

Microemulsions are currently the subject of many investigations because of their wide range of potential and actual utilizations[21]. The high capacity of microemulsions for drugs makes them attractive formulations for pharmaceuticals. Micro emulsions as isotropic, thermodynamically stable transparent (or translucent) systems of oil, water and surfactant, frequently in combination with a cosurfactant with a droplet size usually in the range of 20-200 nm[22]. In addition no creaming or cracking and phase separation as compared to regular emulsion have kinetic stability results ultimately phase separates, thus selected regions of microemulsions also characterized to prove thermodynamic stability[23]. These systems also offer several benefits for oral administration, including increased absorption, improved clinical potency and decreased toxicity[24]. Microemulsions offer a wide range of applications such as targeted drug delivery, sustained drug delivery, controlled drug delivery, enzyme immobilization, enhancing bioavailability, and masking taste[25].

Recent studies have demonstrated that some essential oils (EOs), such as those of garlic, cinnamon, thyme, oregano, clove, basil, coriander, citrus peel, eucalyptus, ginger, rosemary, and peppermint, among others, have antimicrobial activity against bacteria, yeast, and molds. The hydrophilic or hydrophobic character of the EOs is related to their antimicrobial activity, the proportion of the main components in each of them (terpenoids, phenolics, and aldehyde compounds), and the type of microorganism that they might inhibit or inactivate[16]. Essential oils are natural complex mixtures of volatile compounds characterized with strong odor that are stored in cavities, canals, epidermic cells, glandular trichromes and secretory cells within several plant organs, including flower, bud, seed, leaves, herbs, fruits, bark and roots[26]. Essential oils (EOs) are highly volatile and concentrated phytocompounds with a wide range of health benefits that range from being a potential anti-microbial, antioxidant to an anti-inflammatory agent [27]. Regardless of essential oils prevailing use as natural antioxidant and antimicrobial agents, the widespread use of essential oils in foods are currently limited due to their low water solubility, tendency to interact with other food matrices constituents and strong aroma and taste[28]. Incorporation of essential oils into proper delivery systems can overcome these problems. Various well-designed nano-sized colloidal delivery systems such as nanodispersions, nanoemulsions and microemulsions are offered by nanotechnology in order to effectively deliver these functional lipid compounds. It should be noted that the appearance of the food system should be kept changeless after the addition of essential oil, which can also be achieved by proper nano-sized colloidal delivery systems[29].

Microemulsions are efficient nano-sized delivery systems for essential oils. The microemulsion system is an emulsion with a very small globule size of 0.5 to 10 nm capable of penetrating the epidermis[6]. Microemulsions are thermodynamically stable with low viscosity compared to emulsions[30]. Essential oils are usually available in the form of microemulsions and are used by diluting them with various types of vegetable oils and alcohol. It has a relatively low shelf life and absorption on the skin and is thermodynamically unstable with the ability to produce separate phases during storage. Microemulsion delivery systems can be used to overcome these problems and are relatively more effective[25]. Microemulsion have good stability and can be used as carriers of lipophilic compounds[31].

The addition of actives into the essential oil-based microemulsion systems helps to accommodate sufficient quantity of drugs into microemulsion due to the better solubilization potential of microemulsion as a vehicle[32]. Also, essential oil-based drug-loaded microemulsion systems may provide a synergistic effect to the desired therapeutic action of the drug due to the intrinsic biological properties of essential oils. Therefore, in addition to the individual therapeutic benefits essential oils, these oils serve as drug carriers, thus providing dual advantage. microemulsions provide protection to such essential oils as well as the incorporated drugs (decrease their degradation rate)[29]. These systems enhance pharmacological responses of both drug and essential

oils due to their better penetration and retention ability towards the target which is attributed to the nano size distribution of globules s. Drug loaded essential oils based microemulsion have shown favorable results to target follicular casts, neoplasms, macrophages of the reticulo endothelial systems, skin, scalp, microbial cells[33]. The following section details the investigations based on essential oils based drug loaded microemulsion systems to deliver anti-fungal, anti-oxidant and anti-cancer drugs[29].

CONCLUSION:

From the search results a bibliometric analysis related to essential oil microemulsion with data obtained from PubMed and analyzed using R studio and VOSviewer software. The highest number of scientific publications was in China in 2020, totaling 119 publications, where the keyword microemulsions and essential oils occurred 21 and 47 times. The trend of publications related to essential oil microemulsions is expected to continue to increase. Furthermore, research concerning the development of microemulsion preparations as essential oil delivery systems is also increasingly being developed.

CONFLICT OF INTEREST DECLARATION:

This research has no conflict of interest.

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