



Trends and Insights in *Lavandula angustifolia* Research: A Critical Literature Review (CLR) and Bibliometric Analysis of Scopus and PubMed Databases

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ABSTRACT

English Lavender (*Lavandula angustifolia*) is considered one of the major sources of aromatic and pharmaceutical plants, as well as a source of several volatile organic compounds (VOCs). This aromatic plant has been widely studied for its diverse range of applications in the healthcare, cosmetic, and food industries. A critical literature review (CLR) and bibliometric analysis of the Scopus and PubMed databases were conducted, focusing on extracting and analyzing metadata related to publication trends, influential authors and institutions, and the thematic focus of the existing literature. This study reveals three major findings: spikes in research publications in 2006, 2014, and 2020, suggesting heightened interest on *L. angustifolia* research during these periods; significant contributions from the United States, Iran, and China, with prominent institutions like CNRS and Tehran University of Medical Sciences reflecting its global and multidisciplinary appeal; and a wide range of scientific applications, particularly in agricultural sciences, medicine, and biochemistry, with a strong emphasis on peer-reviewed papers and reviews. The study concludes that utilizing VOS-viewer software for bibliometric analyses plays a pivotal role in identifying novel works and collaboration networks, thereby guiding future research directions. This comprehensive analysis underscores *L. angustifolia*'s significant and evolving impact across various scientific fields.

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Introduction

Medicinal plants have historically provided useful natural chemicals with diverse medicinal qualities. Researchers are using *in vitro* approaches to address the increasing demand for herbal medicines and the decreasing availability of these plants. The growing demand for herbal medicines and the dwindling supply of these plants have driven researchers to explore alternative methods of propagation and cultivation, including *in vitro* techniques [4, 22]. *Lavandula angustifolia*, sometimes referred to as English lavender, is a plant that has immense significance in terms of its medical and commercial value. Given its wide geographical range and its valuable attributes in terms of decoration, pharmaceutical, and fragrance, this species contributes significantly to the economies of many countries. *In vitro* production of *L. angustifolia* has been documented as a successful technique to produce many genetically identical plantlets, which may be used to produce valuable bio chemicals [28].

L. angustifolia, sometimes referred to as English lavender, is a very adaptable plant that has attracted considerable interest across several sectors, including horticulture, medicine, and cosmetics. It has a total of 32 species, along with other infraspecific taxa and hybrids [23]. *L. angustifolia* originates from the Mediterranean area, has a significant historical background of customary use, and has subsequently emerged as an essential component in contemporary applications, highlighting its versatile array of advantages. Moreover, *L. angustifolia* has been highly valued in the field of horticulture for its visual attractiveness and pleasant scent. The plant's vivid purple blossoms and subtle scent make it a favored option for landscaping, garden beds, and floral displays.

In vitro propagation, or micropropagation, is a groundbreaking approach in plant production that provides a very efficient and dependable way for safe, sustainable, and mass production of plant components. Enhancements to the micropropagation of economic plants have pronounced economic benefits through reduced losses and waste [27]. Moreover, advancements in biotechnology for propagating ornamental plants

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may enhance characteristics like color, aroma, disease resistance, and vase life. This can result in the development of novel and superior plant types that possess both high aesthetic appeal and commercial value [19]. Numerous studies indicate that biotechnology breakthroughs including tissue culture techniques enhance plant propagation by improving features like color, disease resistance, and yield. They also enable precise genetic alterations and accelerate breeding procedures [14, 6, 7, 28].

A SLR is a rigorous procedure for performing comprehensive evaluations of existing literature. The process includes evaluating different techniques and examining strategies to improve the effectiveness and comprehensiveness of education and research [25]. However, bibliometric studies are considered essential for assessing scientific content. Through the examination of trends in publications, citations, and co-authorship, we may gain useful insights into various academic settings. The use and combination of these two methodologies show that they can positively contribute to literature by offering a full comprehension of the subject matter [26].

The aims of this study are:

- To perform a critical literature review (CLR) to gather insights into the current methodologies, challenges, and breakthroughs on *L. angustifolia*.
- To employ bibliometric analysis to identify research trends and patterns in the literature on *L. angustifolia*.

Material and Methods

Bibliometric Analysis and SLR

Bibliometric analysis is a method used to examine bibliographic data, including articles, books, reviews, and conference papers, particularly in the fields of science, library science, and information science. This analysis often relies on comprehensive databases such as Scopus or Web of Science [24]. Efficient tools for conducting bibliometric and scientometric studies include Bibliometrix, VOS-viewer, and SciMAT. These tools offer unique features and capabilities that can be tailored to meet specific user requirements [17]. The analysis of metrological literature frequently depends on extensive databases like Scopus or Web of Science. Scopus provides extensive coverage across diverse fields and offers access to a wide variety of document types and citation data. This enables detailed analysis of scholarly impact and precise literature searches with high accuracy and retrieval rates [29, 30, 31]. Bibliometric databases like Scopus and PubMed are useful for keyword searches and citation analysis and provide reliable and consistent coverage for making comparisons across different disciplines [8]. Moreover, Dimensions covers 96.42% of Scopus-indexed journals, making it very suitable for doing such analyses [32].

In this research, the Scopus and PubMed databases served as the primary source for both bibliometric analysis and the critical literature review (CLR). Additionally, VOS-viewer version 1.6.20 was utilized to conduct the analysis, leveraging its advanced capabilities for visualizing, and interpreting bibliometric data. For the SCR, the top fifteen articles resulting from the bibliometric analysis were selected from both databases for a more in-depth review. Part of the data collection and analysis was conducted using Microsoft 365, which facilitated the creation of statistical analysis charts. The literature search was executed in the Scopus and PubMed databases in July 2024. To comprehensively retrieve relevant publications, the search results were categorized into four types: (i) articles, (ii) conference papers, (iii) reviews, and (iv) conference reviews. The search formula applied was TITLE-ABS-KEY (title-abstract-keyword), ensuring that any term appearing in the title, abstract, or keywords of a publication would be included in the search results. The specific advanced search strings used in the Scopus and PubMed databases for this study are as follows:

Scopus: TITLE-ABS-KEY (*Lavandula* AND *angustifolia*) OR TITLE-ABS (lavender) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMIT-TO (DOCTYPE , "cp") OR LIMIT-TO (DOCTYPE , "cr"))

PubMed: (*Lavandula angustifolia* [Title/Abstract]) OR (lavender [Title/Abstract]).

Keywords and search terms included in the search formula were: *Lavandula*, *angustifolia*, and lavender. The search results acquired using the described method were saved as a CSV and PubMed file. The relevant files included details such as the author(s), document title, year, source title, citation count, source and document type, affiliations, publisher, correspondence address, author keywords, and indexed keywords. The obtained files were then loaded into VOS-viewer version 1.6.20 software.

Based on the extracted data, the study performed CLR as well as analyses of the following aspects:

- Analysis of documents per year by source
- Analysis of documents per year
- Analysis of documents by country or territory

- Analysis of documents by affiliation
- Analysis of documents by subject area
- Analysis of documents by type
- Citation analysis of documents and authors
- Co-authorship analysis of authors
- Co-occurrence analysis of all keywords.

These analyses enabled the creation of network visualizations, overlay visualizations, and density visualizations, completing the analysis process. The layout and clustering settings were fine-tuned to improve the visual representation, considering the content and data. Larger nodes represent higher connectivity and greater significance. Additionally, some statistical charts were generated using Microsoft 365.

Result and Discussion

Bibliometric Analysis of Scopus Database

Trends in publication output over time

Fig 1 illustrates the publication trends of *L. angustifolia* research across four key journals from 1990 to 2024. Notable peaks in publication numbers are observed in 2006, suggesting a significant research interest or breakthrough during that period, particularly in "Acta Horticulturae," which led to the surge. Subsequent years show fluctuating publication trends with additional peaks around 2014 and in recent years, indicating ongoing but variable interest in the topic. Overall, "Industrial Crops and Products" and "Acta Horticulturae" have been consistent contributors, while "Evidence Based Complementary and Alternative Medicine" and the "Journal of Essential Oil Research" show more sporadic publication activity. This pattern reveals both sustained and episodic research efforts, reflecting the multidisciplinary nature of *L. angustifolia* studies.

Documents per year by source

Compare the document counts for up to 10 sources.

Compare sources and view CiteScore, SJR, and SNIP data

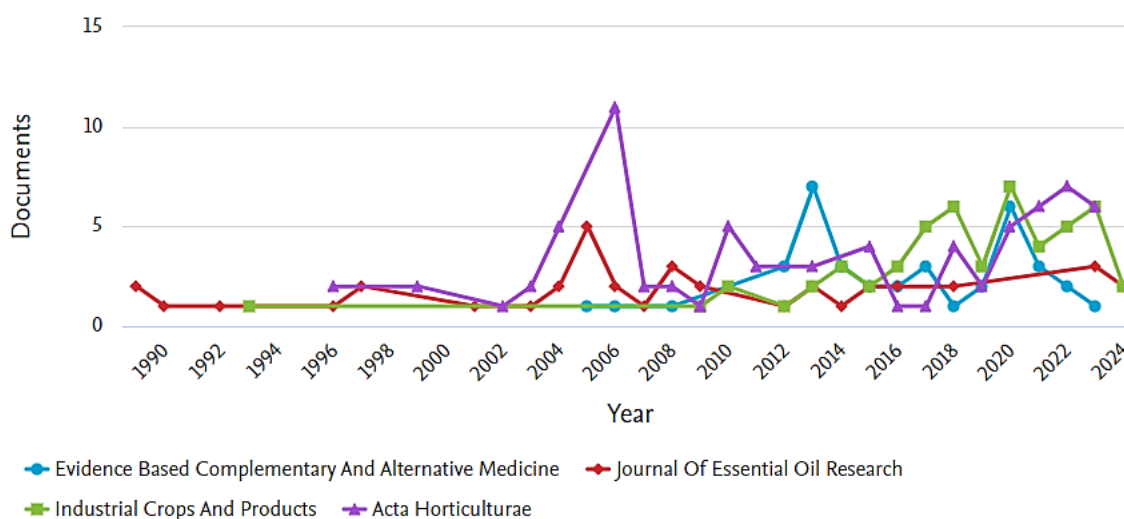


Fig 1 Annual Publication Trends by Journal for *L. angustifolia* Research (1990-2024)

During the early period from 1901 to around 1990, the research output was minimal, maintaining a very low and steady rate of publications. This suggests that *L. angustifolia* was not a major focus of scientific inquiry during these years, possibly due to limited recognition of its potential benefits or a lack of advanced research methodologies. Starting in the early 1990s, there is a noticeable uptick in the number of publications, indicating a growing interest in this plant. This growth phase continues steadily until around 2010, reflecting an increasing awareness of the significance of *L. angustifolia* in various fields such as complementary medicine, essential oils, and horticulture (Fig 2). The consistent rise in publications during this period suggests an expanding body of research and a broadening scope of studies.

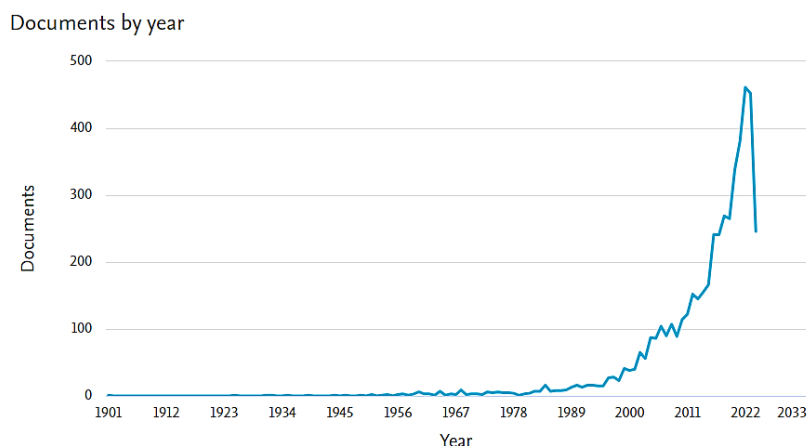


Fig 2 General Publication Trends for *L. angustifolia* Research (1901-2023)

Post-2010, the results show a rapid increase in the number of documents regarding *L. angustifolia* published per year, peaking significantly around 2020. This surge implies a heightened research interest and possibly major breakthroughs or innovations in the study of *L. angustifolia*. The peak around 2020 could also be attributed to an intensified focus on natural and alternative remedies in response to global health trends. However, there is a sharp decline in the number of publications after the peak, which could indicate a saturation point in research or shifts in research funding and priorities

Documents by country or territory

Compare the document counts for up to 15 countries/territories.

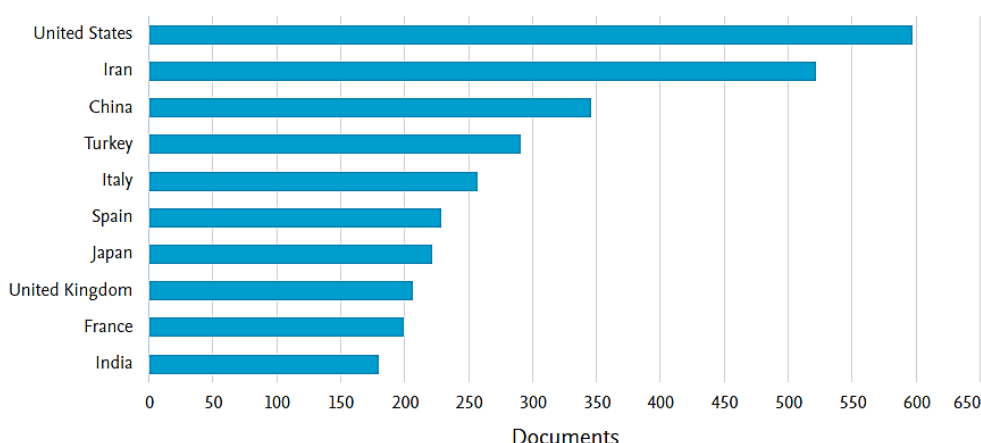



Fig 3 Global Distribution of *L. angustifolia* Research Publications by Country in the Scopus Database (1990-2024)

The United States stands out with the highest number of documents, surpassing 600 publications, indicating a significant research focus and academic interest in *L. angustifolia* within the country. Iran follows closely with nearly 550 documents, reflecting a strong research output in this area as well. China also shows substantial engagement with approximately 450 publications. Türkiye, Italy, and Spain form the next tier of contributors, each with document counts ranging between 250 and 350. This suggests a moderate but significant level of research activity in these countries. Japan, the United Kingdom, and France exhibit similar levels of research output, with each producing between 200 and 250 documents. India, while having the lowest count among the top contributors, still shows considerable research activity with around 200 documents. This indicates that *L. angustifolia* research has a broad international scope, encompassing contributions from various regions around the world. Fig 3 underscores the global nature of research on *L. angustifolia*, with a diverse array of countries actively contributing to the body of knowledge in this field. The high number of publications from multiple countries highlights the widespread scientific interest and the importance of this plant in various research domains.

Documents by affiliation 

Compare the document counts for up to 15 affiliations.

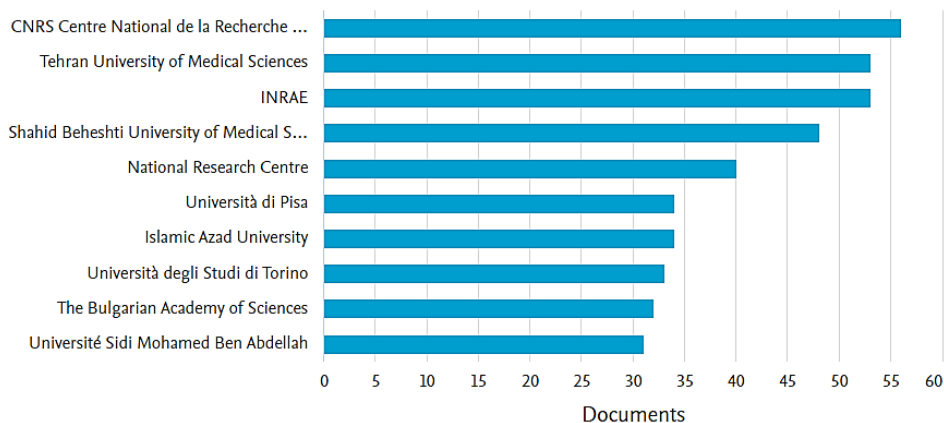


Fig 4 Top Institutional Contributors to *L. angustifolia* Research Publications in the Scopus Database

Fig 4 provides a comparison of the top 10 affiliations contributing to this field. The CNRS Centre National de la Recherche Scientifique (France) is the leading institution with close to 60 documents, highlighting its significant contribution to *L. angustifolia* research. The Tehran University of Medical Sciences (Iran) and INRAE (France) follow closely, each contributing over 50 documents, demonstrating their active involvement in this research area. Other notable institutions include the Shahid Beheshti University of Medical Sciences (Iran) and the National Research Centre (Egypt), both producing around 45 documents. The Università di Pisa (Italy), Islamic Azad University (Iran), and Università degli Studi di Torino (Italy) each have contributed approximately 35 documents, indicating a strong research presence in these universities. The Bulgarian Academy of Sciences (Bulgaria) and the Université Sidi Mohamed Ben Abdellah (Morocco) round out the list with 30 documents each, showing their active participation in *L. angustifolia* research. This distribution underscores the collaborative and international nature of research on *L. angustifolia*, with significant contributions from institutions across Europe, the Middle East, and North Africa.

Fig 5 presents the distribution of research publications related to *L. angustifolia* across various academic disciplines, as recorded in the Scopus database.

Documents by subject area

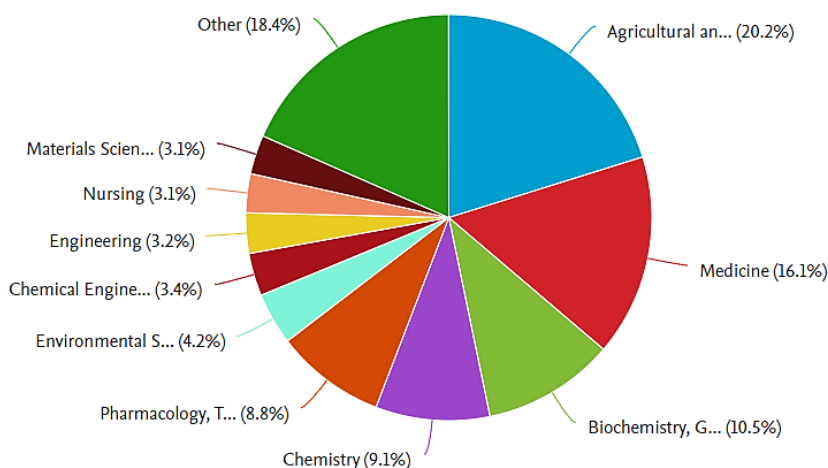


Fig 5 Distribution of *L. angustifolia* Research Publications by Subject Area in the Scopus Database

The largest segment is "Agricultural and Biological Sciences," which accounts for 20.2% of the publications. This reflects the significant interest in the agricultural aspects and biological studies of *L. angustifolia*. "Medicine" follows with 16.1%, indicating a strong focus on the medicinal properties and health-related research of this plant. "Biochemistry, Genetics, and Molecular Biology" represents 10.5% of the documents,

highlighting the molecular and biochemical research conducted on *L. angustifolia*. "Chemistry" constitutes 9.1% of the publications, underscoring the chemical analysis and studies related to this species. "Pharmacology, Toxicology, and Pharmaceutics" also have a notable share with 8.8%, indicating research into the pharmacological effects and potential toxicology of *L. angustifolia*. Other subject areas with significant contributions include "Environmental Science" (4.2%), "Chemical Engineering" (3.4%), "Engineering" (3.2%), "Nursing" (3.1%), and "Materials Science" (3.1%). These fields represent various interdisciplinary applications and studies involving *L. angustifolia*. The "Other" category accounts for 18.4% of the publications, which likely includes various other disciplines contributing to the research on *L. angustifolia*. Nevertheless, Fig 5 demonstrates the diverse range of academic fields engaged in research on *L. angustifolia*, highlighting its multifaceted importance across different scientific domains.

Documents by type

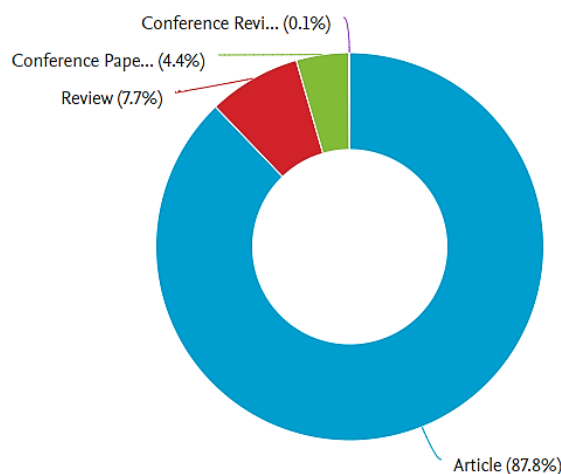


Fig 6 Distribution of *L. angustifolia* Research Publications by Document Type in the Scopus Database

Fig 6 provides a breakdown of the different types of research publications related to *L. angustifolia* in the Scopus database. The data is represented in a donut chart, highlighting the proportion of each document type. Most of the publications are "Articles," which make up 87.8% of the total documents. This indicates that the primary mode of disseminating research findings on *L. angustifolia* is through peer-reviewed journal articles. "Reviews" account for 7.7% of the documents, reflecting a substantial number of publications that synthesize existing research and provide comprehensive overviews on various aspects of *L. angustifolia*. "Conference Papers" constitute 4.4% of the publications, showing the contributions from academic conferences where researchers present their latest findings. "Conference Reviews" are the least represented, making up only 0.1% of the documents. This suggests that review papers specifically presented at conferences are relatively rare in this research area. This result underscores that most *L. angustifolia* research is published in the form of articles and reviews, with a smaller proportion presented at conferences. This distribution highlights the emphasis on rigorous peer-reviewed dissemination in the academic community studying this plant (Fig 6).

Citation Analysis of Documents

Fig 7 visualizes the interconnections between various research papers through citation links, highlighting influential works and clustering related studies based on citation patterns. The network is divided into multiple-colored clusters, each representing a thematic area within *L. angustifolia* research. These clusters indicate groups of documents with high citation interconnectivity, suggesting shared research interests and focus areas. Central nodes within each cluster represent highly cited papers, signifying their influence and foundational role in the research domain.

Notable papers include [16] which is central in its cluster, indicating significant influence, and [3] and [9] which are also highly cited and prominently positioned within their respective clusters. Researchers associated with these highly cited papers, such as [16], [3], and [9], are highlighted as key contributors to the field. Their work forms the backbone of current *L. angustifolia* research and has guided subsequent studies. The centrality and connectivity of their papers in the network emphasize their role in advancing the research landscape. Inter-cluster connections illustrate interdisciplinary research connections, indicating how findings in one thematic area are utilized or referenced in another. This highlights the integrative nature of the research field, where

studies on the chemical properties of lavender, for instance, may link to agricultural practices or therapeutic applications. These connections suggest potential areas for interdisciplinary collaboration, fostering innovation and comprehensive studies. Emerging research areas are also evident in the network, represented by smaller or newer clusters. These areas, while not yet extensively cited, hold potential for future growth and innovation. Researchers can identify these nodes to explore novel topics and contribute to the expanding body of knowledge in *L. angustifolia* research. Ultimately, the citation network provides a comprehensive overview of the most cited papers and influential researchers in *L. angustifolia* research. By examining the clusters, seminal works, and interconnections, researchers can gain valuable insights into the current state of the field, identify critical studies, and explore opportunities for future research and collaboration. This analysis serves as a vital tool for navigating the extensive literature and advancing the knowledge frontier in *L. angustifolia* research.

Analysis of Documents by Author

Fig 8 presents a document network analysis of authors, highlighting their influence based on document counts. Each node in this network represents an author, with the size of the node indicating the volume of the published document. Larger nodes signify more frequently published documents by authors, suggesting their substantial impact within the research domain. The lines connecting the nodes represent citation relationships between authors, with thicker lines indicating stronger document publishing connections. Key observations from the network include:

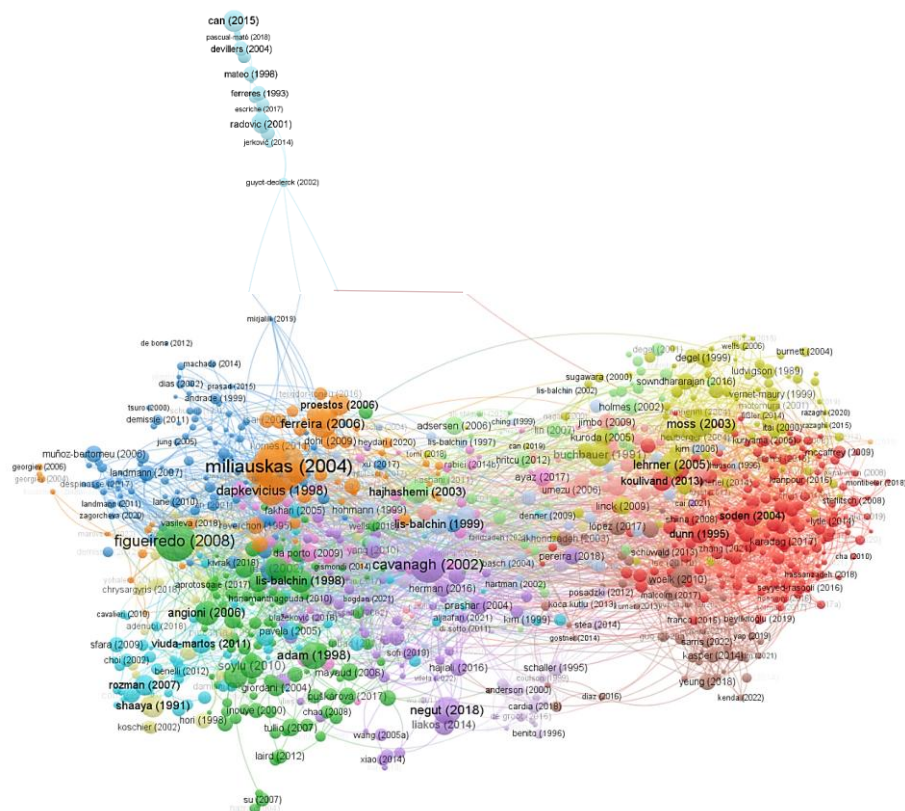


Fig 7 Citation Network Analysis of *L. angustifolia* Research Papers

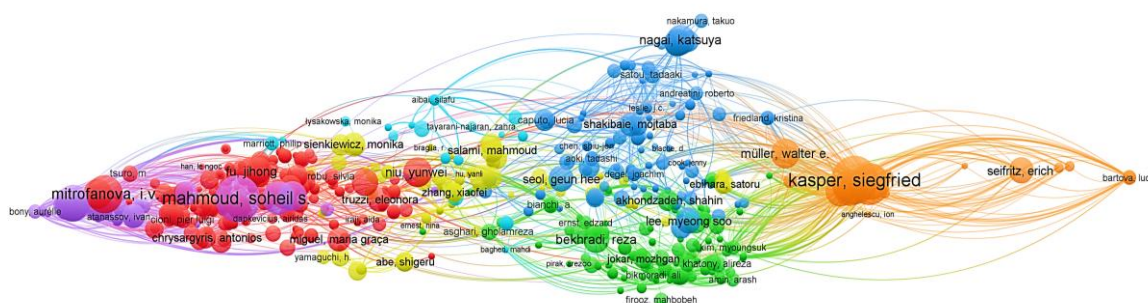


Fig 8 Analysis of documents by Authors

Kasper, Siegfried stands out as a prominent node with extensive connections, indicating a significant citation impact and influence on the research community. Other notable authors include Mahmoud, Soheil S., Volz, H.P, and Mitrofanova, I.V., who are also central Figures in the network with numerous document counts. The network is divided into several colored clusters, each representing groups of authors with strong document interconnections. The clusters highlight the key research areas and the most influential contributors within each area.

Documents by author

Compare the document counts for up to 15 authors.

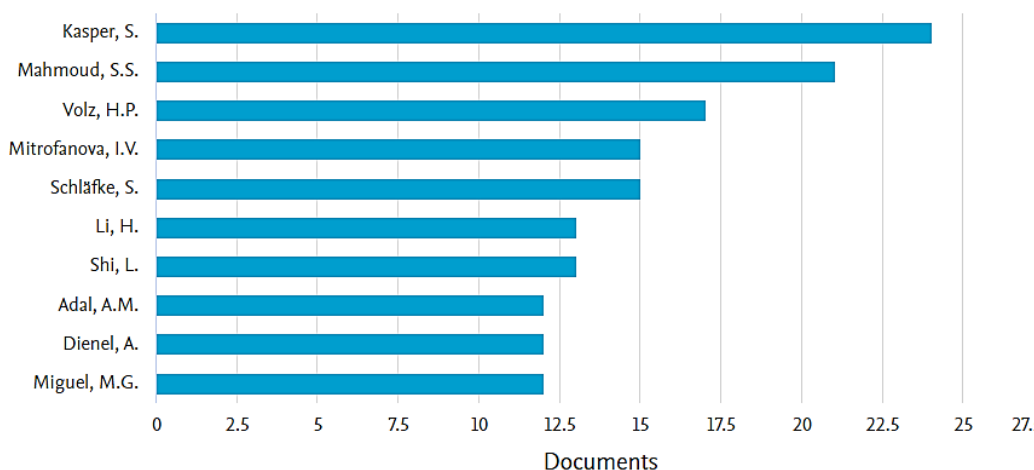


Fig 9 Document Count by Author in *L. angustifolia* Research

These findings underscore the importance of both citation influence and research output in identifying key contributors and understanding collaborative dynamics within the field. This comprehensive analysis highlights the significant roles played by authors like Kasper, Siegfried, Mahmoud, Soheil S., and Mitrofanova, I.V., emphasizing their substantial contributions (Fig 9).

Co-authorship Analysis of Authors

Fig 9 highlights the collaborative relationships among researchers, showing how different authors are connected through co-authored publications. Each node in the network represents an author, with the size of the node indicating the number of co-authored publications. Larger nodes represent authors with a higher number of co-authored works, suggesting they are key collaborators within the field. The lines connecting the nodes represent co-authorship relationships, with thicker lines indicating stronger or more frequent collaborations between authors. The network is divided into multiple-colored clusters, each representing a group of authors who frequently collaborate with one another. Notable clusters include those led by authors such as Zou, Junbo, Yang, Ming, and Wang, [25], who are central Figs within their respective clusters. Zou, Junbo stands out with a large node and numerous connections, indicating a significant role in fostering collaborative research efforts.

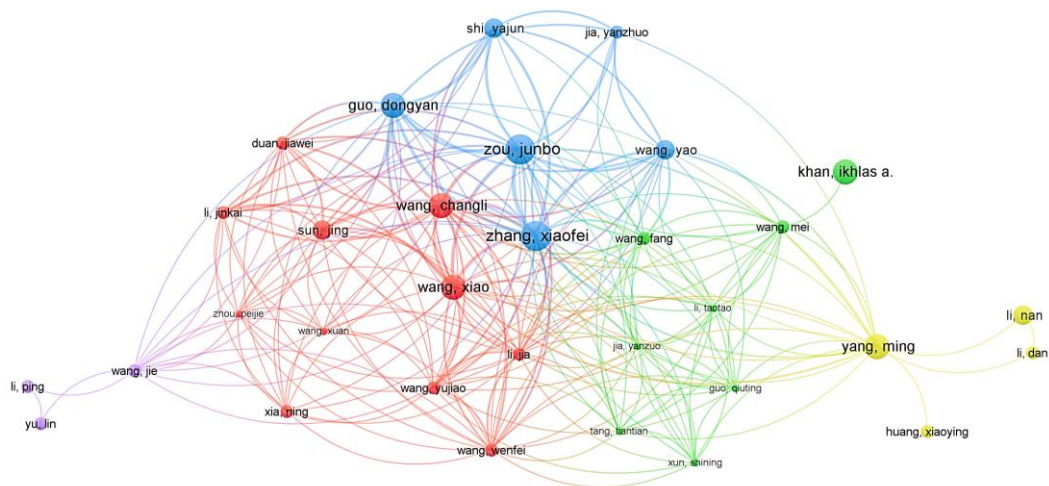


Fig 10 Co-Authorship Network Analysis of Authors in *L. angustifolia* Research

Other prominent authors include Sun, Jing, Li, Jinkai, and Wang, Changli. These researchers have substantial co-authorship networks, suggesting their work is highly collaborative and they play pivotal roles in their research communities. Their central positions within their clusters indicate that they are key facilitators of research collaboration in *L. angustifolia*. Inter-cluster connections illustrate interdisciplinary collaborations and the integration of diverse research perspectives. Authors such as Khan, Ikhlas A. and Yang, Ming have connections spanning multiple clusters, indicating their collaborative efforts extend across different research groups and thematic areas within *L. angustifolia* research. By examining the centrality and connectivity of the nodes, it is clear which researchers are key collaborators and how collaborative efforts are structured within the field. The clusters highlight major collaborative groups and the interconnected nature of the research community, emphasizing the importance of teamwork and interdisciplinary collaboration in advancing the research on *L. angustifolia*.

Co-Occurrence Analysis of All Keywords

The co-occurrence network analysis was conducted with a minimum number of occurrences of a keyword set to 5. Out of the total 31.239 keywords identified, 3.785 keywords met this threshold. Fig 10 shows how different keywords are related based on their co-occurrence in research documents, highlighting key topics and themes within the field.

In the co-occurrence network, each node represents a keyword, with the size of the node indicating the frequency of its appearance across research documents. Larger nodes signify more frequently used keywords, suggesting their importance and centrality within the research domain. The lines connecting the nodes represent the co-occurrence relationships between keywords, with thicker lines indicating stronger or more frequent co-occurrence (Fig 10).

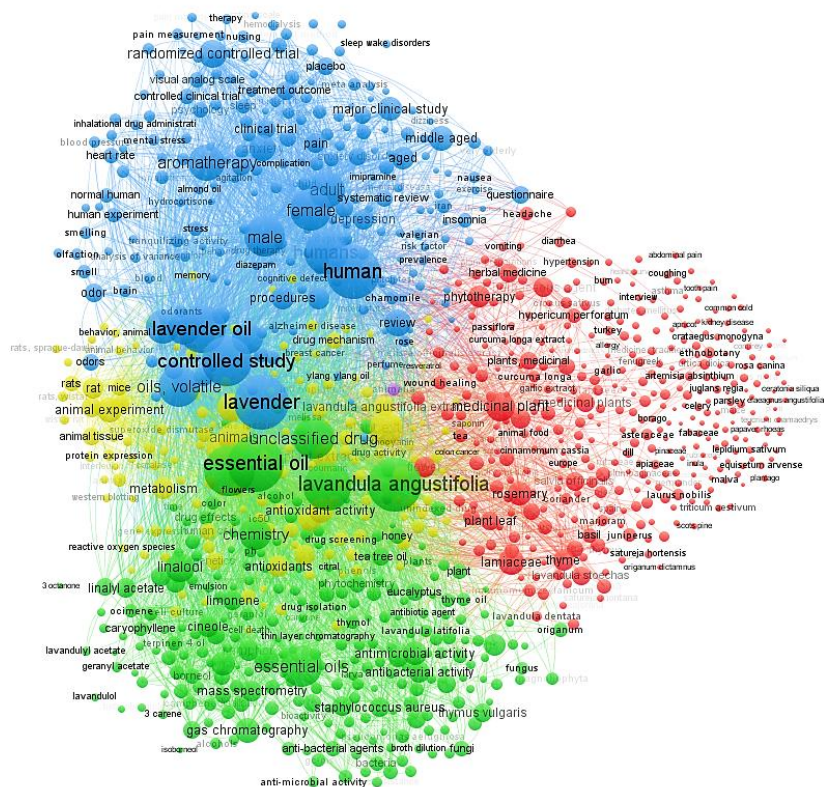


Fig 11 Co-Occurrence Network Analysis of All Keywords

The network is divided into multiple-colored clusters, each representing a group of related keywords that frequently appear together in the literature. Notable clusters include those centered around terms such as "human", "lavender oil", and "essential oil", which are key focal points in *L. angustifolia* research.

- **Human Studies (Blue Cluster):** Keywords such as "clinical trial", "randomized controlled trial", "aromatherapy", and "depression" are prominent in this cluster. This indicates a significant focus on the human health applications and therapeutic benefits of *L. angustifolia*, particularly in clinical and controlled study settings.
- **Chemical and Biological Properties (Green Cluster):** This cluster includes keywords like "essential oil", "antioxidant activity", "chemistry", and "mass spectrometry". The emphasis here is on the chemical composition and biological activities of lavender, including its antioxidant and antimicrobial properties.
- **Phytotherapy and Herbal Medicine (Red Cluster):** Terms such as "phytotherapy", "medicinal plant", and "herbal medicine" dominate this cluster. It highlights the use of *L. angustifolia* in traditional and herbal medicine practices, and its integration with other medicinal plants.
- **Experimental Studies (Yellow Cluster):** Keywords in this cluster, like "animal experiment", "rats", "metabolism", and "volatile oils", suggest a focus on experimental studies involving animal models and the examination of lavender's physiological effects and metabolic pathways.

The central positioning of keywords such as "*Lavandula angustifolia*", "essential oil", and "lavender oil" indicates their broad relevance and connectivity across different research themes. Inter-cluster connections illustrate the interdisciplinary nature of *L. angustifolia* research, where findings in one area, such as chemical properties, may inform and enhance studies in human health applications or experimental models. Through the analysis of pivotal and interconnected keywords, researchers may ascertain the primary areas of concentration, comprehend the interdisciplinary connections, and investigate prospective novel avenues for their investigations. This study is an effective instrument for mapping the research environment and providing guidance for future studies around *L. angustifolia*.

Bibliometric Analysis of PubMed Database

Co-authorship analysis of authors

Co-authorship analysis of authors was conducted with a minimum number of documents of an author set to 1. A total of 8751 authors were identified. Prominent nodes such as Zair, Touriya and Bourhia, Mohammed stand out due to their large sizes, indicating their central roles and numerous co-authorships in PubMed database.

These authors are influential within the research community, having collaborated extensively with others. Their centrality in the network suggests they have contributed significantly to advancing the research on *L. angustifolia* through their numerous collaborative works (Fig 12).

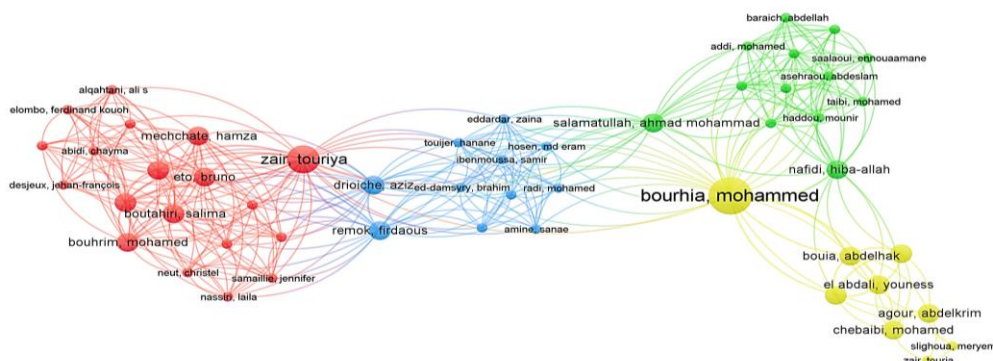


Fig 12 Co-Authorship Network Analysis of Authors in PubMed Database

The network is partitioned into many distinct clusters, each denoting a cohort of writers who engage in regular collaborations. The Red Cluster, led by Zair, Touriya, includes authors like Mechchate, Hamza, Eto, Bruno, and Boutahir, Salima. This cluster is tightly connected, indicating strong collaborative relationships within the group. The Green Cluster, dominated by Bourhia, Mohammed, includes collaborators such as Salamatullah, Ahmad Mohammad, Nafidi, Hiba-Allah, and Bouia, Abdelhak, reflecting a similarly high level of interconnectivity and extensive collaboration. Additionally, the Blue Cluster contains significant authors like Driouiche, Aziz and Remok, Firdaous, highlighting another important collaborative group. Inter-cluster connections are evident, illustrating interdisciplinary collaboration and the integration of diverse research perspectives. For example, Zair, Touriya has connections extending to other clusters, suggesting cross-group collaborations. These inter-cluster connections highlight the interdisciplinary nature of research in *L. angustifolia*, where findings and expertise are shared across different research groups. The dense interconnections within clusters and between key nodes indicate a robust collaborative network. Authors with central positions and numerous connections, such as Zair, Touriya and Bourhia, Mohammed, play pivotal roles in fostering collaboration and driving research forward. This co-authorship network analysis provides valuable insights into the collaborative landscape of *L. angustifolia* research, emphasizing the importance of teamwork and interdisciplinary collaboration in advancing knowledge in this field.

Co-occurrence analysis of all keywords

Co- occurrence analysis of all keywords was conducted with a minimum occurrence of a keyword set to 5. Out of the total 6521 keywords identified, 625 keywords met this threshold. Within the co-occurrence network, every node symbolizes a term, and the node's size corresponds to the frequency of its occurrence in research materials. Nodes of greater size indicate terms that are used more often, indicating their significance and vital role within the study field. The lines that link the nodes in the diagram depict the relationships of co-occurrence between terms. Thicker lines indicate a stronger or more frequent co-occurrence (Fig 12).

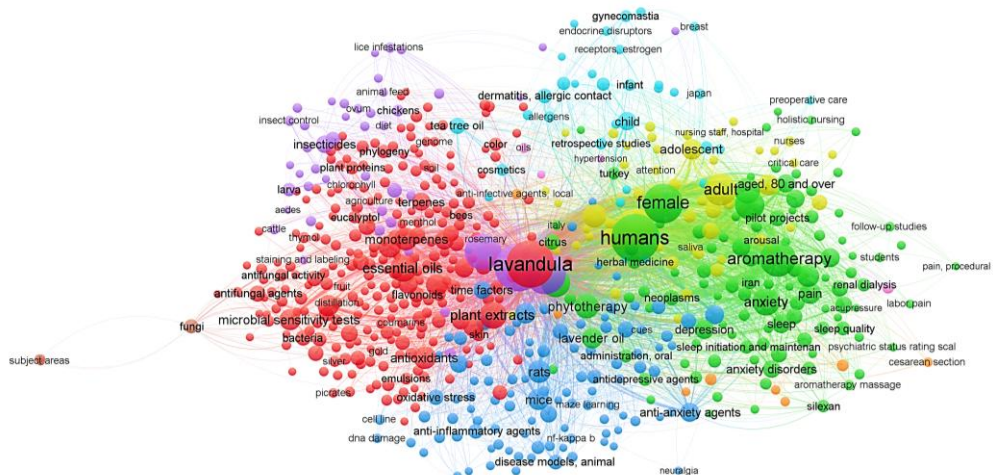


Fig 13 Co-Occurrence Network Analysis of Keywords in PubMed Database

The network is divided into multiple-colored clusters, each representing a group of related keywords that frequently appear together in the literature. Notable clusters include those centered around terms such as "*Lavandula*", "humans", and "aromatherapy", which are key focal points in *L. angustifolia* research.

- **Lavandula and Plant Extracts (Red Cluster):** This cluster includes keywords such as "*Lavandula*", "plant extracts", "essential oils", and "monoterpenes". This suggests a significant focus on the chemical properties, extraction methods, and components of lavender and its essential oils.
- **Human Studies and Health Applications (Green Cluster):** Keywords like "humans", "female", "anxiety", and "aromatherapy" are prominent in this cluster. It indicates a strong emphasis on the health applications of lavender, particularly in human studies related to anxiety, depression, and aromatherapy practices.
- **Experimental and Disease Models (Blue Cluster):** This cluster includes terms such as "rats", "oxidative stress", "antioxidants", and "disease models, animal". The focus here is on experimental studies involving animal models and the examination of lavender's physiological effects and potential therapeutic benefits.
- **Dermatological and Cosmetic Applications (Purple Cluster):** Keywords such as "dermatitis", "allergic contact", "insecticides", and "cosmetics" are found in this cluster, suggesting research interests in the dermatological and cosmetic applications of lavender, including its use in treating skin conditions and as a natural insect repellent.

The central positioning of keywords like "*Lavandula*", "essential oils", and "aromatherapy" indicates their broad relevance and connectivity across different research themes. Inter-cluster connections illustrate the interdisciplinary nature of *L. angustifolia* research, where findings in one area, such as chemical properties, may inform and enhance studies in human health applications or experimental models. Through the analysis of pivotal and associated terms, researchers may ascertain the primary areas of concentration, comprehend the interdisciplinary connections, and investigate prospective novel avenues for their study. This analysis could be an important tool for mapping the research environment and providing guidance for future studies in *L. angustifolia*.

Critical Literature Review (CLR)

For the CLR, a total of 15 articles (10 from Scopus and 5 from PubMed) were selected based on their citation count and connectivity in the network visualization (Fig 7) during the analysis process in VOS-viewer.

1. Miliuskas, G., 2004 [16]:

This study investigates the antioxidant properties of extracts from 12 medicinal and aromatic plants through radical scavenging assays using DPPH and ABTS. The study aims to identify potential sources of natural antioxidants for various applications like food and cosmetics. The plants studied include various species of *Salvia*, *Lavandula*, *Calendula*, *Matricaria*, *Echinacea*, *Rhaponticum*, *Juglans*, *Melilotus*, *Geranium*, and *Potentilla*.

Methodologically, dried plant materials were extracted using acetone, ethyl acetate, and methanol. Radical scavenging activity was evaluated using spectrophotometric assays, correlating these activities with the content of total phenolic compounds, flavonoids, and flavonols in the extracts. Key findings from this study include:

1. **Radical Scavenging Activity:** Methanol extracts generally exhibited higher radical scavenging activity compared to acetone and ethyl acetate extracts. Particularly, extracts from *Geranium macrorrhizum* and *Potentilla fruticosa* showed very high activity in both DPPH and ABTS assays, surpassing the well-known antioxidant *Salvia officinalis*.
2. **Correlation with Phenolic Compounds:** There was a positive correlation between the radical scavenging capacities of the extracts and their total phenolic compound content. This suggests that phenolic compounds are likely major contributors to the observed antioxidant activity.
3. **Differences Between Assays:** While there was generally good correlation between DPPH and ABTS assays, some plants showed different levels of activity in each assay. *Echinacea purpurea*, for instance, exhibited higher activity in the ABTS assay compared to the DPPH assay.

2. Cavanagh, H. M. A., & Wilkinson, J. M., 2002 [3]:

This research explores the various biological activities of lavender essential oil, examining its therapeutic and cosmetic applications, and highlights the challenges in evaluating its effectiveness due to methodological issues.

Lavender essential oil, derived from species such as *L. angustifolia*, *L. latifolia*, *L. stoechas*, and *Lavandula x intermedia*, has been traditionally used for its purported antibacterial, antifungal, carminative, sedative,

antidepressive, and insect repellent properties. The review investigates the scientific evidence supporting these claims and identifies areas needing further research. Lavender oil demonstrates activity against various bacteria and fungi, including antibiotic-resistant strains like MRSA and VRE. However, the efficacy of lavender oil varies significantly with different types and origins of lavender, as well as the methods of extraction and testing. Some studies suggest lavender oil is effective as a topical agent but not for deep-seated infections.

The study mentioned that aromatherapy using lavender oil is linked to reduced anxiety, improved mood, and enhanced sleep quality in various clinical settings. The oil's components, such as linalool and linalyl acetate, are thought to have sedative effects through their actions on the central nervous system. Additionally, lavender oil has been traditionally used for wound healing and treating skin conditions such as eczema and psoriasis. It may also help reduce discomfort post-labor when added to bath water. Nonetheless, there are concerns about allergic reactions and skin irritation, though some studies suggest lavender is less likely to cause dermatitis compared to other essential oils. Lavender oil has also shown potential as a pesticide and in promoting hair growth in conditions like alopecia. Its use in midwifery and palliative care for pain relief and anxiety reduction has been explored, although more rigorous scientific studies are needed to substantiate these claims. The review highlights several methodologies used in studying lavender oil's effects. Methods like disc/well diffusion and agar/broth dilution are commonly used in antimicrobial testing, though they are not always suitable for essential oils due to their hydrophobic nature. Clinical trials, such as those assessing hair growth and anxiety reduction, are mentioned. However, inconsistencies in methodologies and small sample sizes often limit these studies' reliability. Techniques like gas chromatography with mass spectrometry (GC/MS) are used to determine the composition of lavender oils, which is crucial for understanding their varying biological activities.

The main challenges in evaluating the therapeutic potential of lavender oil include variability in oil composition. Differences in species, extraction methods, and geographical origins lead to significant variability in oil composition, complicating the assessment of its biological activities. Methodological inconsistencies, such as the lack of standardized methodologies and detailed reporting in studies, make it difficult to compare results and draw definitive conclusions. There is a call for standardized, reproducible methods to assess essential oils' biological activities accurately.

The article concludes that while lavender essential oil shows promise in various therapeutic applications, more rigorous and standardized scientific research is needed to fully understand and validate its biological activities and clinical potential.

3. Figueiredo, A. C., et al., 2008 [9]:

This study examines the various factors that influence the presence, yield, and composition of secondary metabolites in plants, particularly focusing on volatile components and essential oils. The study identifies several key variables that can affect these secondary metabolites from their formation in the plant to their eventual isolation. These factors are critically analyzed to optimize cultivation conditions and harvesting times for commercially important crops, aiming to produce higher yields of high-quality essential oils that meet market standards.

The researchers found that understanding the chemical variability and yield determinants is essential not only for commercial purposes but also for using essential oils and volatiles as chemotaxonomic tools. The factors influencing the chemical variability and yield include physiological variations, environmental conditions, geographic variations, genetic factors and evolution, political and social conditions, and the amount of plant material, space, and manual labor required.

The methodology employed in the study involved a comprehensive review of the factors affecting secondary metabolite production in plants. This included analyzing physiological and environmental conditions, geographic and genetic variations, and socio-political influences. The research underscores the importance of each factor in determining the quality and yield of essential oils, highlighting the complexity of optimizing cultivation practices to meet both commercial and scientific needs.

4. Dapkevicius, A., et al., 1998 [5]:

This article investigates the potential of several aromatic herbs grown in Lithuania as sources of natural antioxidants in response to the growing demand for natural additives over synthetic ones. The herbs examined include marjoram (*Majorana hortensis* Moench), catnip (*Nepeta cataria* L.), oregano (*Origanum vulgare* L.), lavender (*Lavandula angustifolia* Mill), thyme (*Thymus vulgaris* L.), hyssop (*Hyssopus officinalis* L.), anise hyssop (*Lophanthus anisatus* Benth), and sage (*Salvia officinalis* L.).

To evaluate their antioxidant potential, dried herb samples underwent extraction using supercritical CO₂, acetone, methanol/water, and hydro-distillation. Additionally, deodorized herb samples (after the removal of essential oils) were extracted with acetone. The antioxidant activities of these extracts, essential oils, and dried

deodorized aqueous extracts were assessed using the β -carotene bleaching test through diffusion and spectrophotometric methods.

The findings indicated that the highest yields of extracts were obtained using polar solvents. Specifically, thyme and sage acetone oleoresins exhibited significant antioxidant activity in the tests conducted, suggesting that these two herbs are the most promising sources of natural antioxidants among the samples tested. The methodology included the use of various extraction techniques to isolate potential antioxidant compounds from the herbs, followed by rigorous testing of these extracts' antioxidant activities. The study highlights the effectiveness of polar solvents in yielding extracts with high antioxidant potential, particularly emphasizing the promise of thyme and sage as valuable natural sources of antioxidants.

5. Adam, K., et al., 1998 [2]:

The study explores the antifungal properties of essential oils from four plant species: *Origanum vulgare* subsp. *hirtum*, *Mentha spicata*, *Lavandula angustifolia*, and *Salvia fruticosa*, against human pathogens *Malassezia furfur*, *Trichophyton rubrum*, and *Trichosporon beigelii*. Among these, *O. vulgare* subsp. *hirtum* oil demonstrated the highest fungicidal activity, achieving a 95% reduction in the number of metabolically active cells at a dilution of 1/50000 within 6 hours of exposure. The main components of these essential oils, carvacrol and thymol, were identified as having the highest levels of antifungal activity. The therapeutic efficacy of *O. vulgare* subsp. *hirtum* essential oil was further validated through experiments on rats infected with *T. rubrum*, showing promising results. Additionally, the essential oils were assessed for mutagenic activity using the Ames test and were found to be non-mutagenic.

The methodology involved:

- Testing the antifungal properties of essential oils against specific human pathogens.
- Identifying and analyzing the main components of the oils for their antifungal activity.
- Conducting in vivo experiments to assess therapeutic efficacy.
- Using the Ames test to evaluate potential mutagenic effects.

The findings underscore the significant antifungal potential of *O. vulgare* subsp. *hirtum* essential oil, particularly due to its components carvacrol and thymol, and confirm its safety in terms of non-mutagenicity.

6. Lehrner, J., et al., 2005 [13]:

The study aimed to examine the effects of essential oils of orange and lavender on anxiety, mood, alertness, and calmness in dental patients. The research involved 200 patients aged 18 to 77 years, equally divided between men and women. Participants were randomly assigned to one of four groups: ambient odor of orange, ambient odor of lavender, music, or a control condition (no odor, no music).

While waiting for their dental procedures, patients' anxiety, mood, alertness, and calmness were measured. Statistical analyses indicated that both ambient odors of orange and lavender significantly reduced anxiety and improved mood compared to the control condition. The methodology included:

- Randomly assigning patients to different sensory conditions (orange odor, lavender odor, music, control).
- Assessing emotional states (anxiety, mood, alertness, calmness) while patients waited for dental treatment.
- Conducting statistical analyses to compare the effects of the different conditions.

The findings support the notion that ambient odors can influence emotional states, suggesting that the use of essential oils, particularly orange and lavender, can be beneficial in reducing anxiety and improving mood in dental patients.

7. K. Benachour, K., 2017 [10]:

The study conducted an inventory of insects visiting *Lavandula officinalis* flowers over three years (2009, 2010, and 2013) in the Constantine region of northeast Algeria. Researchers recorded insects from three orders: Hymenoptera, Lepidoptera, and Diptera. Most taxa identified (81%) exhibited very low average abundances (≤ 1 individual/day), with 73% being bees, including the honeybee (*Apis mellifera*), the bumblebee (*Bombus terrestris*), *Ceratina cucurbitina*, and two *Megachilidae* species, *Anthidium florentinum* and *A. manicatum*.

The study found that bees had higher visitation rates than Lepidopterans, which included *Iphiclides podalirius*, *Pieris rapae*, and *Polyommatus dorylas*. Quantitative analysis, based on abundance and visitation rates, identified *B. terrestris* and *A. mellifera* as the most dominant pollinators of *L. officinalis*. Qualitative analysis, which involved counting pollen grains on the bodies of the five major bee species, revealed that *B. terrestris* was not only the most dominant but also the most efficient pollinator.

The methodologies used in the study included:

- Long-term observation and recording of insect visits to *L. officinalis* flowers over multiple years.
- Quantitative analysis of insect abundance and visitation rates.

- Qualitative analysis of pollen grains transported by major pollinators to assess pollination efficiency. The findings underscore the significant role of bees, particularly *B. terrestris* and *A. mellifera*, in the pollination of *L. officinalis*, with *B. terrestris* being the most efficient pollinator due to its high dominance and pollen transport capacity.

8. Abuhamdah, S., & Chazot, P. L., 2008 [1]:

The article explores the potential of natural therapeutics, specifically essential oils, as a strategy for treating emotional and neurodegenerative disorders. It highlights the historical and ongoing relevance of deriving novel treatments from natural sources, particularly in addressing the limitations of current medications for anxiety, depression, and psychotic disorders, which often suffer from inefficacy and multiple side effects. The review focuses on essential oils from Melissa and Lavender plants, noting their beneficial properties in alleviating emotional disorders. Melissa oil is particularly noted for its dual benefits: reducing agitation and maintaining attention in patients with dementia. Lavender oil is also recognized for its anti-agitation properties.

The methodology of the review involves examining existing evidence on the efficacy of these essential oils in treating emotional and neurodegenerative disorders. The analysis indicates that both Melissa and Lavender essential oils offer promising alternative treatments, particularly in neurodegenerative disease contexts where current medications fall short. In summary, the article emphasizes the therapeutic potential of Melissa and Lavender essential oils in managing emotional disorders and highlights their specific benefits for patients with neurodegenerative diseases. Their findings suggest a valuable role for natural therapeutics in addressing the shortcomings of conventional medications.

9. Lane, A., et al., 2010 [12]:

This study aims to develop *L. angustifolia* as a model system to investigate the molecular regulation of essential oil production, which comprises mono- and sesquiterpenes. As an initial step towards establishing the necessary genomic tools for this species, researchers constructed two cDNA libraries from lavender leaves and flowers and sequenced 14,213 high-quality expressed sequence tags (ESTs). The EST collection includes orthologs for genes involved in the 1-deoxy-D-xylulose-5-phosphate (DXP) and mevalonic acid (MVA) pathways of terpenoid biosynthesis, as well as known terpene synthases and prenyl transferases.

To understand the regulation of terpene metabolism in lavender flowers, the study evaluated the transcriptional activity of genes encoding 1-deoxy-D-xylulose-5-phosphate synthase (DXS) and HMG-CoA reductase (HMGR) in glandular trichomes (oil glands) using real-time PCR. The results showed that HMGR transcripts were barely detectable, while DXS was highly expressed in glandular trichomes, suggesting that essential oil constituents are predominantly produced through the DXP pathway in these tissues. Additionally, the gene responsible for linalool production (linalool synthase, LinS) was strongly expressed in glandular trichomes.

Interestingly, the most abundant transcript in floral glandular trichomes corresponded to a sesquiterpene synthase (cadinene synthase, CadS), even though sesquiterpenes are minor constituents of lavender essential oils. This finding, along with the weak activity of the MVA pathway (the primary route for sesquiterpene production) in trichomes, suggests that precursor supply might be a limiting factor in sesquiterpene biosynthesis in lavender flowers.

Methodologies:

- Construction of cDNA Libraries: Libraries were constructed from lavender leaves and flowers.
- Sequencing and EST Collection: Sequencing yielded 14,213 high-quality ESTs.
- Homology Analysis: ESTs were analyzed for homology to sequences in GenBank to identify genes involved in terpenoid biosynthesis.
- Transcriptional Activity Evaluation: Real-time PCR was used to evaluate the transcriptional activity of DXS and HMGR in glandular trichomes.
- Gene Expression Analysis: Expression levels of LinS and CadS were assessed in floral glandular trichomes.

Findings:

- Essential oil production in lavender glandular trichomes predominantly occurs through the DXP pathway, indicated by high DXS expression.
- LinS, responsible for linalool production, is strongly expressed in glandular trichomes.
- Despite being the most abundant transcript, CadS expression suggests a bottleneck in sesquiterpene biosynthesis due to limited precursor supply from the MVA pathway.

This research provides a foundation for further genomic studies on lavender, aiming to enhance the understanding of essential oil biosynthesis and regulation in plants.

10. Yahya, M.A., et al., 2024a [28]:

The article details the development of an *in vitro* propagation protocol for *L. angustifolia* Miller. Researchers used Murashige and Skoog (MS) media supplemented with various concentrations of Plant Growth Regulators (PGRs) to study the growth parameters of nodal segments and assess callus formation and shoot proliferation. Nodal explants supplemented with 2 mg/L of 6-Benzylaminopurine (BAP) successfully formed callus. The optimal hormonal concentration for shoot proliferation from callus cultures (39.33%) was determined to be 5 mg/L of 2-Isopentenyl adenine (2iP). Additionally, the best media for callus growth were found to be those containing 1 and 2 mg/L of BAP, achieving a 98% formation rate.

The researchers performed qualitative and quantitative analyses on the callus cultures and *in vitro* propagated seedlings, examining phenolic profiles, flavonoids, and phenolic acids using High-Performance Liquid Chromatography (HPLC), as well as analyzing volatile compounds through headspace-SPME. Seedlings grown in media with 1 mg/L of 6-Furfurylamino purine (KIN) had the highest yield of phenolic acids (11.95 ± 0.01 mg GAE/g). Conversely, the lowest concentration of phenolic acids (2.17 ± 0.04 mg GAE/g) was found in media containing 0.5 mg/L of BAP and 0.5 mg/L of Naphthaleneacetic acid (NAA).

The study also revealed that plantlets grown in media with 0.5 mg/L of BAP and 0.5 mg/L of NAA exhibited the highest flavonoid yield (31.67 ± 0.06 μ g/g QE/g), whereas callus samples in media supplemented with 0.5 mg/L of BAP had the lowest flavonoid yield (11.59 ± 0.02 μ g/g QE/g). HPLC analysis showed variability in phenolic acid content among callus cultures and plantlets, identifying gallic acid, 4-OH benzoic acid, chlorogenic acid, vanillic acid, caffeic acid, cinnamic acid, and rosmarinic acid as the main constituents. Headspace-SPME analysis identified twenty-two chemicals, with eucalyptol, nonanal, borneol, carvone, and β -caryophyllene being the most abundant. The study concludes that micropropagation of *L. angustifolia* is an effective method for producing large quantities of genetically identical plantlets to produce high-value bio compounds.

11. Nakajima, D., et al., 2024 [18]:

The study aimed to explore the relationship between oxytocin secretion and the effects of aromatherapy with lavender oil on anxiety levels in healthy individuals. The hypothesis was that if aromatherapy could promote oxytocin secretion, it might improve mood and alleviate anxiety. The investigation was carried out through a randomized open crossover trial involving 15 men and 10 women. Each participant experienced both a placebo intervention (control group) and an aromatherapy session (aromatherapy group). The aromatherapy intervention included a 30-minute session in a room with diffused lavender oil followed by a 10-minute hand massage using a carrier oil containing lavender oil.

Anxiety levels were measured using the State-Trait Anxiety Inventory (STAI) at three time points: before the intervention, 30 minutes after the start of the intervention, and after the hand massage. Saliva samples were collected at the same time points to measure oxytocin levels.

The findings revealed that in women, both aromatherapy and hand massage independently led to a reduction in anxiety levels and an increase in salivary oxytocin levels after aromatherapy. In men, anxiety levels decreased following both aromatherapy and hand massage, regardless of the presence of lavender oil, but there were no significant changes in salivary oxytocin levels between the control and aromatherapy groups during the intervention period. Furthermore, a positive correlation was found between anxiety levels and salivary oxytocin levels before the intervention, which shifted to a negative correlation after the hand massage with lavender oil. In conclusion, the study suggests that aromatherapy with lavender oil effectively reduces anxiety and increases oxytocin levels in women, whereas in men, aromatherapy's impact on anxiety and oxytocin levels is less clear, though it does alter the correlation between anxiety and oxytocin. These findings indicate that the effects of aromatherapy can vary by sex, highlighting the need for further research to understand the underlying mechanisms and potential sex-specific responses.

12. Mazraeh, A., Tavallali, H., & Tavallali, V., 2024 [15]:

The article investigates the synthesis of copper nano complexes (Cu-NCs) using aqueous extracts of jujube and neem leaves and examines their effects on *Lavandula sublepidota* Rech. f., an Iranian native medicinal herb. Copper (Cu) is recognized as an essential micronutrient in plant physiology and biochemistry. The study aimed to determine the impact of foliar application of Cu-jujube and Cu-neem Cu-NCs at various concentrations (0, 10, 25, and 50 mg L⁻¹) on the bioactive compounds, antioxidant capacity, and essential oil content of the lavender plant.

The methodology involved synthesizing Cu-NCs from jujube and neem leaf extracts and applying these complexes as foliar sprays to the lavender plants. The concentrations used were 0, 10, 25, and 50 mg L⁻¹. The researchers then measured several parameters, including levels of flavonoids and polyphenols, essential oil yield, secondary metabolite content, antioxidant activity, and antibacterial activity against three pathogen strains.

The findings revealed that the highest levels of flavonoids and polyphenols were observed in plants treated with Cu-NCs at a concentration of 25 mg L⁻¹, with no significant difference between the effects of Cu-jujube and Cu-neem complexes. Additionally, at the same concentration, the essential oil yield increased by 48% with Cu-jujube and 52% with Cu-neem compared to the control. This suggests an optimal concentration threshold, beyond which toxicity effects may occur. The study also reported that the amount of commercially significant secondary metabolites was highest at the 25 mg L⁻¹ concentration compared to 10 and 50 mg L⁻¹. Moreover, the maximum antioxidant activity was found in lavender extracts treated with 25 mg L⁻¹ Cu-NCs. The exogenous application of Cu-NCs significantly enhanced the antibacterial activity of the extracts against the three pathogen strains, demonstrating greater effectiveness at the optimal concentration of 25 mg L⁻¹. In conclusion, the study suggests that Cu-NCs, particularly at a concentration of 25 mg L⁻¹, are effective in enhancing the production of essential oil and bioactive compounds in *Lavandula sublepidota* Rech. f. This research highlights the importance of synthesizing nano complexes using plant extracts and emphasizes the potential for using plant-based Cu-NCs to increase the medicinal and commercial value of lavender through improved yields of essential oils and bioactive compounds. The results underscore the necessity of understanding the phytochemical changes in lavender plants resulting from such treatments.

13. Kim, Y. J., et al., 2024 [11]:

The article addresses the ongoing health issue of smoking in patients with type 2 diabetes mellitus by investigating the impact of high glucose (HG) and nicotine on intracellular calcium ion concentrations ([Ca²⁺]_i) in microglia, neurons, and astrocytes. The study's primary objective was to compare [Ca²⁺]_i levels in these cells under HG and nicotine conditions and to evaluate the potential modulatory effects of *L. angustifolia* Mill. essential oil (LEO).

The researchers employed Fura-2 acetoxymethyl ester fluorescence to measure [Ca²⁺]_i concentrations. Their results showed that treatment with HG and nicotine significantly increased [Ca²⁺]_i in microglia and neurons through Ca²⁺ influx from extracellular sources. Notably, LEO was found to significantly reduce this increased Ca²⁺ influx in microglia, an effect that was partially inhibited by the Na⁺/Ca²⁺ exchanger (NCX) inhibitor Ni²⁺. Similarly, in neuron-like cells pretreated with HG and nicotine, LEO significantly decreased Ca²⁺ influx, with this effect partially blocked by the L-type Ca²⁺ channel blocker nifedipine and the T-type Ca²⁺ channel blocker mibefradil. Additionally, the study found that either LEO treatment or a two-fold increase in the number of astrocytes attenuated the Ca²⁺ influx caused by high glucose and nicotine in mixed cultures of microglia, neuron-like cells, and astrocytes. These findings suggest that LEO can regulate HG and nicotine-induced Ca²⁺ influx into microglia and neurons through distinct mechanisms, highlighting its potential therapeutic role in mitigating the cellular effects of smoking in diabetic patients.

14. Shan, J., et al., 2024 [20]:

In this study researchers utilized a replicative lifespan (RLS) experiment involving K6001 yeast to identify anti-aging compounds in lavender extract (*L. angustifolia* Mill.), leading to the discovery of β-cyclocitral (CYC) as a promising anti-aging agent. Concurrent validation was achieved through chronological lifespan (CLS) experiments with YOM36 yeast and mammalian cells, confirming the anti-aging properties of CYC. This compound was shown to extend the yeast lifespan and inhibit cell senescence induced by etoposide (ETO).

The study delved into the mechanisms underlying CYC's anti-aging effects, focusing on telomere biology, oxidative stress, and autophagy. Administration of CYC resulted in significant increases in telomerase content, telomere length, and expression levels of telomeric shelterin proteins, including telomeric-repeat binding factor 2 (TRF2) and repressor activator protein 1 (RAP1). Furthermore, CYC reversed H₂O₂-induced telomere damage, highlighting its potent antioxidant capacity. It also improved the survival rate of BY4741 yeast under oxidative stress induced by 6.2 mM H₂O₂ by enhancing antioxidant enzyme activity and reducing levels of reactive oxygen species (ROS), reactive nitrogen species (RNS), and malondialdehyde (MDA). Moreover, CYC was found to enhance autophagic flux and the expression of free green fluorescent protein (GFP) in the YOM38-GFP-ATG8 yeast strain, suggesting an upregulation of autophagy. However, CYC did not extend the RLS of K6001 yeast mutants deficient in antioxidant enzymes (Δ*sod1*, Δ*sod2*, Δ*cat*, Δ*gpx*) or autophagy-related genes (Δ*atg2*, Δ*atg32*), indicating that its anti-aging effects are dependent on these pathways.

These findings collectively reveal that CYC functions as an anti-aging agent by modulating telomeres, oxidative stress, and autophagy. The promising results warrant further investigation of CYC as a potential therapeutic compound for aging-related interventions.

15. Soden, K., et al., 2004 [21]:

The research explores the use of aromatherapy and massage in patients with advanced cancer, focusing on their physical and psychological benefits. Given the growing popularity of these therapies in palliative care,

the study aimed to compare the effects of four-week courses of aromatherapy massage and massage alone on various symptoms in this patient group. Forty-two patients were randomly assigned to three groups: one receiving weekly massages with lavender essential oil and an inert carrier oil (aromatherapy group), one receiving massages with an inert carrier oil only (massage group), and one receiving no intervention.

The outcome measures included a Visual Analogue Scale (VAS) for pain intensity, the Verran and Snyder-Halpern (VSH) sleep scale, the Hospital Anxiety and Depression (HAD) scale, and the Rotterdam Symptom Checklist (RSCL). The study found no significant long-term benefits of either aromatherapy or massage in terms of pain control, anxiety, or overall quality of life. However, there were notable improvements in sleep scores in both the massage and combined massage (aromatherapy and massage) groups. Additionally, the massage group showed statistically significant reductions in depression scores.

The results indicate that the addition of lavender essential oil did not enhance the beneficial effects of massage. Nevertheless, the findings suggest that patients experiencing high levels of psychological distress may derive the most benefit from these therapies. Overall, while aromatherapy did not show added advantages, massage alone was effective in improving sleep and reducing depression in patients with advanced cancer.

Conclusion

This study demonstrates notable patterns and key elements across time, showcasing both enduring and fluctuating interest in the research around *L. angustifolia*. The growing interest in alternative and complementary medicine in response to lifestyle diseases and antibiotic resistance has driven increased research in the medicinal uses of lavender. Additionally, the shift in research funding toward biotechnology and sustainable agricultural practices has contributed to advances in lavender cultivation techniques. The publication patterns show distinct spikes in research effort, particularly in 2006, 2014, and 2020. These peaks suggest periods of increased interest, possibly driven by significant advancements or global health phenomena. The 2006 spike corresponds to major advances in the extraction and commercialization of lavender essential oils, particularly for medical and cosmetic purposes. The 2014 increase can be attributed to a surge in research on natural antioxidants, driven by the global push for more sustainable health solutions. The sharp rise in 2020 is likely linked to the COVID-19 pandemic, where there was a global shift toward exploring alternative remedies and herbal treatments. This aspect provides a more comprehensive understanding toward social, economic, and scientific factors that potentially influence research activity. Publications such as "Acta Horticulturae" and "Industrial Crops and Products" have consistently made contributions, while others have shown more irregular activity, highlighting the wide appeal of the research within multidisciplinary studies. An examination of geographic distribution (Scopus and PubMed databases) reveals that the United States, Iran, and China are the primary publishers, indicating a significant worldwide interest. Institutional analysis highlights prominent actors such as the CNRS in France and Tehran University of Medical Sciences. The examination of subject areas highlights *L. angustifolia*'s wide range of scientific uses, with notable contributions from fields like agricultural sciences, medicine, and biochemistry. The distribution of document types shows that peer-reviewed papers and reviews are the most prevalent, highlighting the strong emphasis on academic rigor in studying Lavender. This study suggests that using citation and co-authorship analysis in Vos-viewer software, researchers may identify pivotal works and authors, as well as reveal crucial collaboration networks as well as researchers can then use this data to inform and steer future research endeavors. In conclusion, this study offers a thorough and inclusive examination of the research environment using Vos-viewer software, highlighting the *L. angustifolia*'s substantial and ever-changing influence on various scientific fields.

Abbreviations

2,2-diphenyl-1-picrylhydrazyl (DPPH); Critical Literature Review (CLR); Centre National de la Recherche Scientifique (CNR); 2,2'-azino-bis 3-ethylbenzothiazoline-6-sulfonic acid (ABTS); High-quality expressed sequence tags (ESTs); Mevalonic acid (MVA); 1-deoxy-D-xylulose-5-phosphate synthase (DXS); HMG-CoA reductase (HMGR); High-performance liquid chromatography (HPLC); State-Trait Anxiety Inventory (STAI); Copper nano complexes (Cu-NCs); High glucose (HG); β -cyclocitral (CYC); Replicative lifespan (RLS); Chronological lifespan (CLS); Visual Analogue Scale (VAS); Snyder-Halpern (VSH); Hospital Anxiety and Depression (HAD); Rotterdam Symptom Checklist (RSCL).

Availability of data and material

Please contact the corresponding author for any data request.

References

1. Abuhamdah, S., and P. L. Chazot, Lemon balm and lavender herbal essential oils: old and new ways to treat emotional disorders?. *Current Anaesthesia & Critical Care*, 2008. 19(4), 221-226.
2. Adam, K., et al., Antifungal activities of *Origanum vulgare* subsp. *hirtum*, *Mentha spicata*, *Lavandula angustifolia*, and *Salvia fruticosa* essential oils against human pathogenic fungi. *Journal of agricultural and food chemistry*, 1998. 46(5), 1739-1745.
3. Cavanagh, H. M. A., and J. M. Wilkinson, Biological activities of lavender essential oil. *Phytotherapy research*, 2002. 16(4), 301-308.
4. Chen, C. C., et al., *In vitro* propagation and analysis of secondary metabolites in *Glossogyne tenuifolia* (Hsiang-Ju)-a medicinal plant native to Taiwan. *Botanical Studies*, 2004. 55, 1-9.
5. Dapkevicius, A., et al., Antioxidant activity of extracts obtained by different isolation procedures from some aromatic herbs grown in Lithuania. *Journal of the Science of Food and Agriculture*, 1998. 77(1), 140-146.
6. Davison, B., et al., The impact of biotechnological advances on the future of US bioenergy. *Biofuels*, 2015. 9. <https://doi.org/10.1002/bbb.1549>.
7. Enfissi, E., et al., New plant breeding techniques and their regulatory implications: An opportunity to advance metabolomics approaches.. *Journal of plant physiology*, 2021. 258-259, 153378 . <https://doi.org/10.1016/j.jplph.2021.153378>.
8. Falagas, M., et al., Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. *The FASEB Journal*, 2007. 22, 338 - 342. <https://doi.org/10.1096/fj.07-9492LSF>.
9. Figueiredo, A. C., et al., Factors affecting secondary metabolite production in plants: volatile components and essential oils. *Flavour and Fragrance journal*, 2008. 23(4), 213-226.
10. Benachour, K., Insect visitors of lavender (*Lavandula officinalis* L.): Comparison of quantitative and qualitative interactions of the plant with its main pollinators. *African Entomology*, 2007. 25(2), 435-444.
11. Kim, Y. J., et al., *Lavandula angustifolia* Mill. inhibits high glucose and nicotine-induced Ca²⁺ influx in microglia and neuron-like cells via two distinct mechanisms. *Biomedicine & Pharmacotherapy*, 2024. 177, 117062.
12. Lane, A., et al., A genomics resource for investigating regulation of essential oil production in *Lavandula angustifolia*. *Planta*, 2010. 231, 835-845.
13. Lehrner, J., et al., Ambient odors of orange and lavender reduce anxiety and improve mood in a dental office. *Physiology & Behavior*, 2005. 86(1-2), 92-95.
14. Limera, C., et al., New Biotechnological Tools for the Genetic Improvement of Major Woody Fruit Species. *Frontiers in Plant Science*, 2017. 8. <https://doi.org/10.3389/fpls.2017.01418>.
15. Mazraeh, A., H. Tavallali and V. Tavallali, Variations in the biochemical characteristics of *Lavandula sublepidota* Rech. f. in response to the foliar enrichment of green-synthesized copper nano complexes from extract of Neem and Jujube. *Plant Physiology and Biochemistry*, 2024. 108885.
16. Miliuskas, G., et al., Screening of radical scavenging activity of some medicinal and aromatic plant extracts. *Food chemistry*, 2024. 85(2), 231-237.
17. Moral-Muñoz, J., et al., Software tools for conducting bibliometric analysis in science: An up-to-date review. *El Profesional de la Información*. 2020. <https://doi.org/10.3145/epi.2020.ene.03>.
18. Nakajima, D., et al., Sex differences in the effects of aromatherapy on anxiety and salivary oxytocin levels. *Frontiers in Endocrinology*, 2024. 15, 1380779.
19. Noman, A., et al., Biotechnological Advancements for Improving Floral Attributes in Ornamental Plants. *Frontiers in Plant Science*, 2017. 8. <https://doi.org/10.3389/fpls.2017.00530>.
20. Shan, J., et al., β -Cyclocitral from *Lavandula angustifolia* Mill. Exerts Anti-Aging Effects on Yeasts and Mammalian Cells via Telomere Protection, Antioxidative Stress, and Autophagy Activation. *Antioxidants*, 2024. 13(6), 715.
21. Soden, K., et al., A randomized controlled trial of aromatherapy massage in a hospice setting. *Palliative medicine*, 2004. 18(2), 87-92.
22. Tasheva, K., and G. Kosturkova, Role of biotechnology for protection of endangered medicinal plants. *Environmental biotechnology-New approaches and prospective applications*, 2013. 235-238.
23. Upson, T., The taxonomy of the genus *Lavandula* L. In *Lavender 2002*. pp. 16-48. CRC Press.
24. Van Eck, N., and L. Waltman, Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics*, 2009. 84, 523 - 538. <https://doi:10.1007/s11192-009-0146-3>
25. Xiao, Y., and M. Watson, Guidance on conducting a systematic literature review. *Journal of Planning Education and Research*, 2017. 39, 112 - 93. <https://doi:10.1177/0739456X17723971>
26. Yahya, M. A., and H. Mammadzada, Targeting generation Z: A systematic literature review (SLR) and bibliometric analysis for effective marketing. *Journal of Politics Economy and Management*, 2024c. 7(1), 21-44.
27. Yahya, M. A., et al., *In vitro* production of *Phalaenopsis* orchids. *Turkish Journal of Biodiversity*, 2024b. 7(1), 41-53. <https://doi.org/10.38059/biodiversity.1452374>
28. Yahya, M.A., et al., Phenolic profile and volatiles of *in vitro* propagated *Lavandula angustifolia* mill. seedlings. *Phyton-International Journal of Experimental Botany*, 2024a. 93(3), 427-444. <https://doi.org/10.32604/phyton.2024.046271>
29. Vieira, E., and J. Gomes, A comparison of Scopus and Web of Science for a typical university. *Scientometrics*, 2009. 81, 587-600. <https://doi:10.1007/s11192-009-2178-0>
30. Burnham, J., Scopus database: a review. *Biomedical Digital Libraries*, 2006. 3, 1. <https://doi:10.1186/1742-5581-3-1>
31. Zhu, J., and W. Liu, A tale of two databases: the use of Web of Science and Scopus in academic papers. *Scientometrics*, 2020. 123, 321-335. <https://doi:10.1007/s11192-020-03387-8>
32. Singh, V., et al. The journal coverage of Web of Science, Scopus and Dimensions: A comparative analysis. *Scientometrics*, 2020. 126, 5113-5142. <https://doi:10.1007/s11192-021-03948-5>