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Sesquiterpenoids in *Aquilaria* oil and their medicinal insights: A structured review

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ABSTRACT

Aquilaria oil, widely used in traditional Chinese medicine, has long been valued for its aromatic and therapeutic properties in treating ailments such as pain, inflammation, and fever. Despite extensive studies on its sesquiterpenoid content, the full medicinal potential of these compounds remains underexplored. This structured review systematically analyzed 177 articles from Scopus and Web of Science, of which 18 met the inclusion criteria, focusing on three main themes: biological activities, chemical characterization, and ethnobotanical and medicinal insights. The findings show that sesquiterpenoids in *Aquilaria* oil are predominantly humulane- and eudesmane-type compounds, frequently linked to anti-inflammatory, antimicrobial, and anticancer properties. Current trends also highlight growing use of DNA barcoding and chemical profiling for species authentication and oil quality evaluation. Moreover, ethnobotanical evidence consistently supports its role as a sedative and immune-modulating agent, increasingly validated by pharmacological studies. Collectively, these insights underscore the therapeutic relevance of *Aquilaria* sesquiterpenoids and identify promising pathways for drug discovery and sustainable utilization.

Keywords: *Aquilaria*; sesquiterpenoids; agarwood; gaharu; chemical compound

1. INTRODUCTION

Aquilaria malaccensis, commonly known as agarwood, is an Asian tree with significant traditional medicinal uses, particularly due to the sedative, antidepressant, and anxiolytic activities of its oil constituents and inhaled vapor (Ahmaed et al., 2022). The phytochemical composition of agarwood, including the presence of sesquiterpenoids, has been a subject of research due to its potential pharmacological significance (Beckmann et al., 2022; Harneti et al., 2022; Nurhaslina et al., 2018; Tajuddeen et al., 2023). The rich biodiversity of plant species has long been a source of inspiration for scientific exploration, particularly in the realm of discovering novel compounds with therapeutic properties. Among the vast array of botanical treasures, *A. malaccensis* stands out as a reservoir of bioactive compounds, prominently featuring sesquiterpenoids. Sesquiterpenoids are a class of secondary metabolites that have been widely studied for their anti-inflammatory, antimicrobial, and anticancer properties (Chen et al., 2022; Eissa et al., 2020; Huo et al., 2019; Yu et al., 2020; Zhang et al., 2023). In the context of *A. malaccensis* oil, these sesquiterpenoids contribute not only to the distinctive fragrance of agarwood but also to its potential therapeutic efficacy. Hence, understanding the composition and pharmacological activities of these sesquiterpenoids holds promise for uncovering new avenues in drug discovery and development (Mahabob et al., 2022).

Sesquiterpenoids are $C_{15}H_{24}$ compounds, formed from three isoprene (C_5H_8) units and can occur in acyclic, exocyclic, or endocyclic forms (Alamil et al., 2022). These compounds are predominantly identified as the primary active constituents in agarwood, the resinous heartwood derived from *Aquilaria* or *Gyrinops*, both belonging to the Thymelaeaceae family (Lei et al., 2019). Traditionally, wood and/or its oil have been extensively utilized in traditional medicine for therapeutic purposes, serving as sedatives, analgesics, and digestive aids, as well as being employed in preparing traditional medicine ingredients for culinary use. Additionally, the wood is used as incense in religious ceremonies and as a fragrant material for aromatherapy in Southeast Asia and the Middle East (Xie et al., 2021). Historically, phytochemical investigations have primarily focused on agarwood originating from *Aquilaria* species, resulting in the isolation of sesquiterpenoids and *2-(2-phenylethyl)* chromones (Haqmi Abas et al., 2020). Notably, sesquiterpenes with distinct colors contribute to the varied qualities of agarwood oil. For instance, 4β,7α-H-eremophil-9(10)-ene-12,13-diol manifests as colorless oil, while 4β,7α,8α-H-eremophil-9(10)-ene-8,12-epoxy-11α,13-diol presents as yellow oil (Haqmi Abas et al., 2020; Xie et al., 2021). Beyond their aromatic properties, sesquiterpenoids have garnered attention in medicinal research. Numerous studies have underscored their significance in treating conditions such as cancer, inflammatory diseases, and infectious diseases (Alamil et al., 2022; Mahabob et al., 2022; Zhang et al., 2023). Investigations into sesquiterpenoids isolated from marine organisms have explored their pharmacological activities and mechanisms of action (Dai et al., 2021). Furthermore, sesquiterpenoids exhibit potential as anticancer agents, influencing cell proliferation, apoptosis, and angiogenesis, and show promise as therapeutic agents for inflammatory diseases like arthritis and colitis (Gozari et al., 2021; Jiang et al., 2021). By shedding light on the sesquiterpenoid composition of *A. malaccensis* oil and exploring its medicinal potential, we aspire to contribute to the growing body of knowledge that may inspire future drug discovery and development breakthroughs.

Research on the essential oil extracted from *A. malaccensis* has gained momentum, particularly due to the presence of sesquiterpenoids, a class of secondary metabolites with diverse biological activities. A comprehensive review (Gao et al., 2019) explored the bioactivities of sesquiterpenoids derived from various natural sources, emphasizing their anti-inflammatory, antimicrobial, and anticancer properties. While the review encompassed sesquiterpenoids from diverse botanical origins, it laid the groundwork for understanding the potential therapeutic implications of similar compounds in *A. malaccensis* oil (Gao et al., 2019; Li et al., 2022).

Studies by Sarih et al. (2021) and Wu et al. (2012) have collectively reported the isolation of several sesquiterpenoids and 2-(2-phenylethyl)-4H-chromen-4-one derivatives from *A. malaccensis* agarwood chips. These investigations identified four novel sesquiterpenoids alongside two previously known compounds, thereby enriching the understanding of the chemical diversity present in *A. malaccensis* oil. Another study presented the first concise synthesis of naturally occurring aquilanols A and B, two unprecedented 7/10 bicyclic sesquiterpenoids isolated from the agarwood of *A. malaccensis* (Wu et al., 2012). The review of volatile and semi-volatile constituents of agarwood, mainly *A. malaccensis, A. sinensis*, and *A. crassna*, also identified mostly sesquiterpenoids, chromones, and volatile aromatic compounds (Naef, 2011; Lloren, 2023). The most recent systematic review evaluated different inoculation strategies for agarwood-producing species and examined the available agarwood-producing species in the literature. The review revealed that *Aquilaria sinenses (A. sinenses)* was the widely utilized specimen for agarwood experiments, while *A. malaccensis* was the country-diverse species in the review (Lloren, 2023).

Previous studies and literature reviews on the sesquiterpenoids of *A. malaccensis* oil and its medicinal insights have provided valuable insights into the phytochemical composition and potential medicinal properties of this species. In a study on the phytochemical screening and characterization of *A. malaccensis,* it was discovered that the agarwood of this species contains various compounds, including sesquiterpenoids. It has been traditionally used for medicinal purposes, exhibiting sedative, antidepressant, and anxiolytic activities (Ahmaed et al., 2022). The presence of sesquiterpenoids in *A. malaccensis* agarwood has been confirmed through comprehensive spectral analyses and chromatography techniques displayed in Figure 1 (Gogoi et al., 2023). Furthermore, the potential medicinal properties of the oil constituents and inhaled vapor of *A. malaccensis,* attributed to its sesquiterpenoid content, have been highlighted in the literature (Ahmaed et al., 2022).

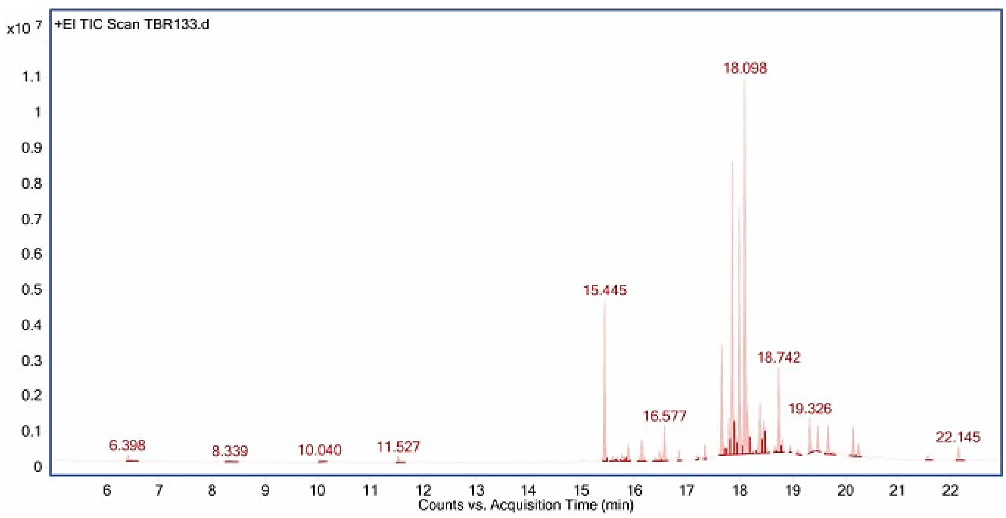

Figure 1. Chromatogram of essential oil from *A. malaccensis* (Gogoi et al., 2023)

Agarwood contains a minimum of 210 sesquiterpenes with diverse skeletal structures, encompassing eudesmanes, eremophilanes, guaianes, agarospiranes, acoranes, cadinanes, prezizaanes, zizaanes, and humulanes. Isolated sesquiter-penes from agarwood are classified into various categories, such as acoranes, agarospiranes, cadinanes, eudesmanes, eremophilanes, guaianes, humulanes, prezizaanes, and zizaanes. The intricate composition of agarwood highlights the significance of sesquiterpenes and chromone derivatives in quality control analysis. Figure 2 illustrates the distribution of sesquiterpene types in agarwood resin, showcasing the predominant presence of eudesmanes (55%), guaianes (53%), and eremophilanes (32%) in the resin. Other notable sesquiterpenes include agarofurans (15%), agarospiranes (14%), and candinanes (3%) (Gao et al., 2019).

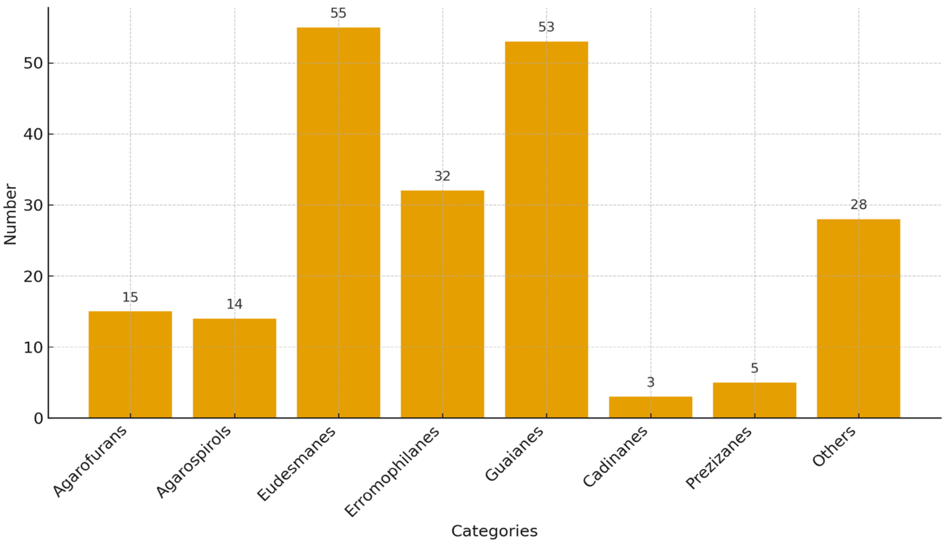

Figure 2. Types of sesquiterpenes in agarwood (Gao et al., 2019)

A phytochemical analysis of agarwood from an *Aquilaria* plant was conducted in a previous study, leading to the isolation and identification of 10 α-glucosidase inhibitory sesquiterpenoids. This set included six newly discovered sesquiterpenoids, namely agarozizanol A to F (1-6), along with four previously known sesquiterpenoids (refer to Figure 3) (Yang et al., 2019). The sesquiterpenoids and chromones in the figure have a variety of biological activities. For example, some of them have been demonstrated to inhibit the growth of cancer cells, while others have been proven to have anti-inflammatory and antibacterial properties (Yang et al., 2019).

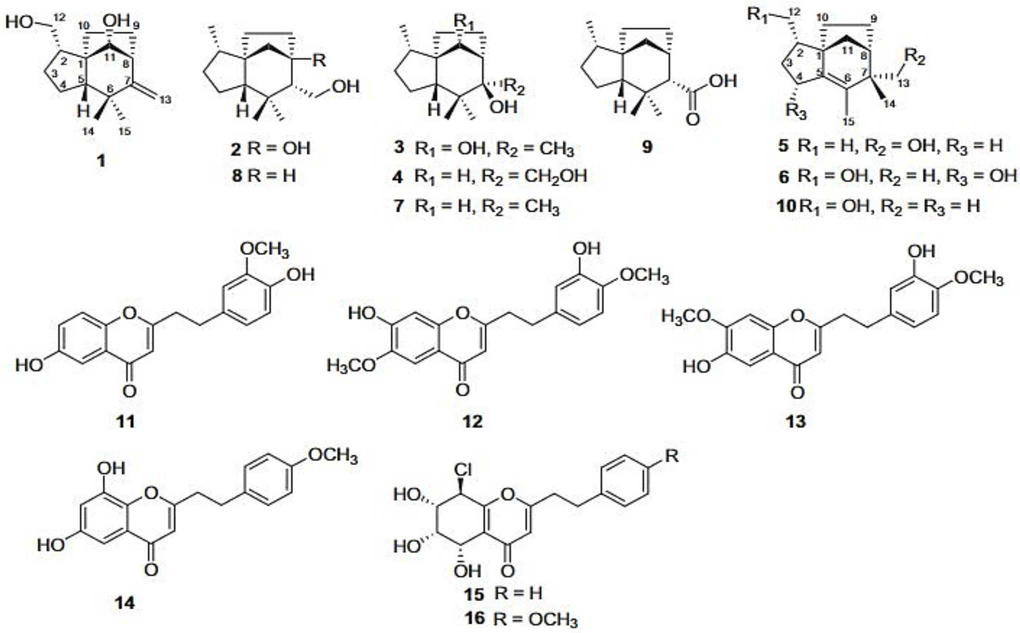

Figure 3. Structures of sesquiterpenoids (Yang et al., 2019)

In addition, a review on the development of agar (*A. malaccensis*) cultivation documented the existing cultivation technology and its potential as an agroforestry component. The review emphasized the economic potential of agarwood production, which is related to the presence of sesquiterpenoids and other valuable compounds in *A. malaccensis* (Talucder et al., 2016). This further supports the importance of understanding the sesquiterpenoid composition of *A. malaccensis* oil for its economic and medicinal implications. Overall, the existing literature provides substantial evidence of the presence of sesquiter-penoids in *A. malaccensis* oil and its potential medicinal insights. These findings can serve as a valuable foundation for further research and the development of high-impact articles on the subject.

2. METERIALS AND METHODS

2.1 Identification

The systematic review procedure for selecting relevant publications involves three key stages. In the initial stage, keywords and synonymous terms were identified using thesauri, dictionaries, encyclopedias, and previous research. Search strings were then crafted from the Scopus and Web of Science databases, as provided in Table 1, and all relevant keywords were identified. A total of 177 publications from both databases were gathered for the current study project in the initial phase of the systematic review procedure.

Table 1. Search strings

Scopus	TITLE-ABS-KEY ((sesquiterpenoids OR agarwood OR 4quilaria OR gaharu) AND medical) AND (LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2023)) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article")) AND (LIMIT-TO (PUBSTAGE, "final")) AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (SRCTYPE, "j"))
Web of Science	(sesquiterpenoids OR agarwood OR 4quilaria OR gaharu) AND medical (Topic) and 2023 or 2022 (Publication Years) and Article (Document Types) and English (Languages)

2.2 Screening

During the screening step, potentially relevant research materials were scrutinized to ensure they aligned with the predefined research questions. Criteria included relevance to sesquiterpenoids and agarwood. This phase involves eliminating all duplicate papers from the initially retrieved list. The initial screening phase resulted in the exclusion of 144 publications. In contrast, the subsequent phase involved the assessment of 33 papers based on distinct inclusion and exclusion criteria outlined in this study (refer to Table 2). The primary criterion for inclusion was literature (research papers), as it serves as the principal source for practical recommendations. This encompassed reviews, meta-synthesis, meta-analyses, books, book series, chapters, and conference proceedings not considered in the most recent study. Additionally, the review focused exclusively on English-language publications, emphasizing that the analysis solely concentrated on the years 2022 and 2023. In total, 115 publications were dismissed due to duplication criteria.

Table 2. Selection criterion in searching

Criterion	Inclusion	Exclusion
Language	English	Non-English
Timeline	2022 – 2023	< 2022
Literature type	Journal (article)	Conference, book, review
Publication stage	Final	In press

2.3 Eligibility

In the third step, termed eligibility, a compilation of 23 articles was assembled. This stage involved a meticulous examination of the titles and key content of all articles to ascertain their alignment with the inclusion criteria and relevance to the current research objectives. Consequently, five reports were excluded for reasons such as being out of the study scope, lacking significant titles, having abstracts unrelated to the study's objective, and lacking full-text access supported by empirical evidence. Ultimately, 25 articles met the criteria and are now available for review, as displayed in Figure 4.

2.4 Data abstraction and analysis

In this study, an integrative analysis served as one of the assessment strategies to scrutinize and amalgamate various research designs, predominantly employing quantitative methods. The objective of this proficient examination was to pinpoint relevant topics and subtopics. The initial phase of theme development commenced with data collection, as depicted in Figure 4, illustrating the authors' meticulous analysis of a compilation of 18 publications for content pertinent to the study's topics. The authors systematically assessed noteworthy studies pertaining to sesquiterpenoids and agarwood in the context of medical insight, examining methodologies and research findings. Subsequently, collaborative efforts among the authors led to the formulation of themes grounded in the evidence presented in this study. A comprehensive log documented analyses, perspectives, or other insights relevant to data interpretation throughout the analytical process. Following this, a thorough comparison of results was conducted to identify any inconsistencies in the theme design process. Notably, in cases of conceptual disagreements, the authors engaged in internal discussions to resolve them. The resulting themes underwent adjustments to ensure coherence.

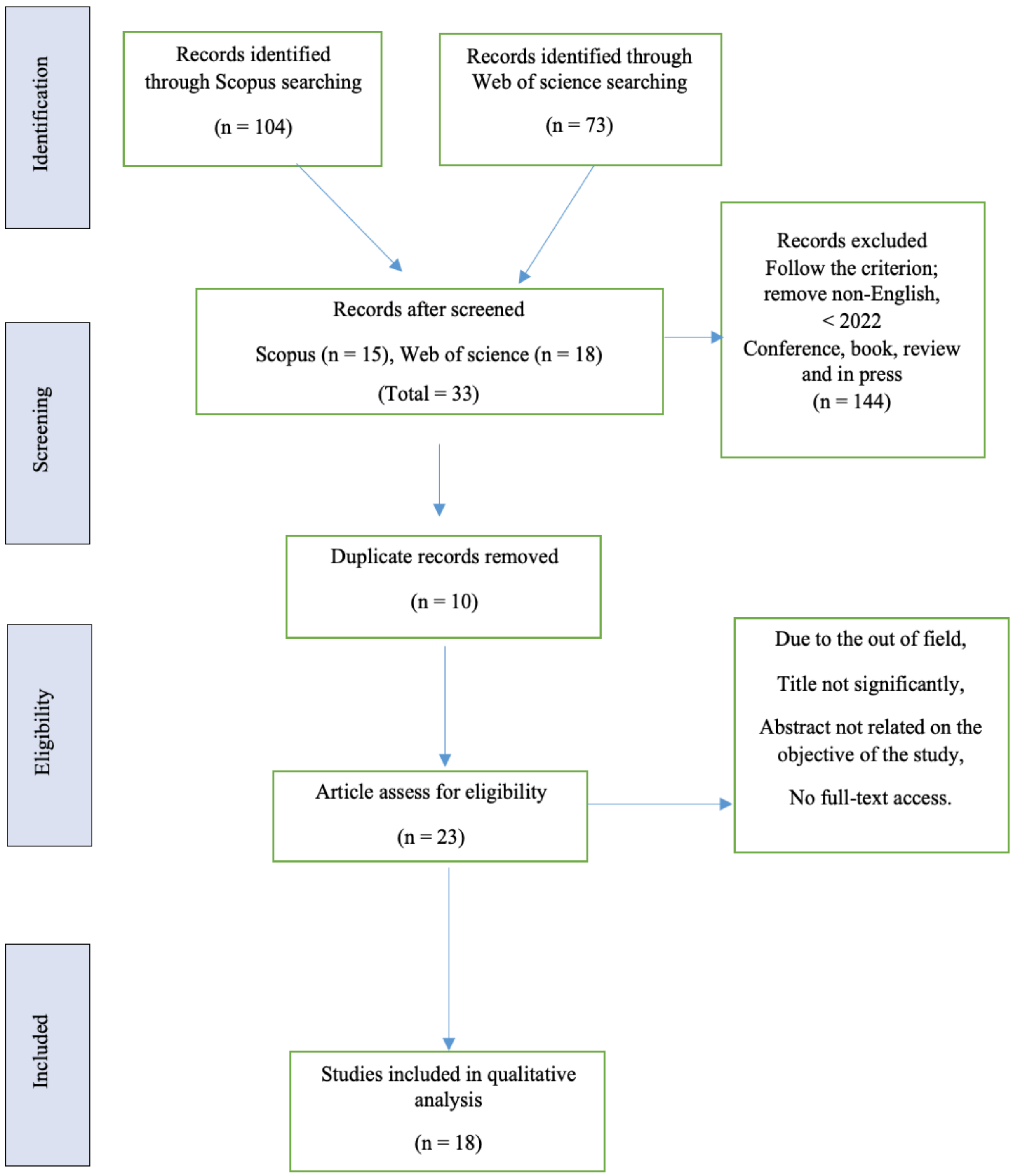

Figure 4. Flow diagram for the proposed study (Mustafa et al., 2022)

2.4.1 Appraisal of quality

Three distinguished experts were meticulously selected to review and validate the 18 articles, each specializing in a unique domain: chemistry compounds with a specific focus on sesquiterpenoids, comprehensive analysis, and expertise in agarwood studies. This critical expert review phase was instrumental in establishing domain validity, ensuring unparalleled clarity, significance, and appropriateness for each subtheme. The study employed the rigorous Critical Appraisal Skills Program (CASP) checklist, comprising eight meticulously defined criteria (refer to Table 3). Quality appraisal was conducted by highly qualified experts with over a decade of extensive experience in the agarwood field and validation. The CASP checklist served as a meticulous guide for evaluating the studies' quality, allowing for a critical examination of various types of evidence, as outlined by Long in 2020 (Long et al., 2020). The three-tiered indicators: excellent, good, and moderate, were employed for the quality appraisal, scrutinizing each article for the clear articulation of research aims, the relevance of methods and research design, appropriateness of recruitment strategy, precision in data collection, rigor in data analysis, lucidity in stating findings, and the overall value of the research, as detailed in Table 3. Ultimately, the 23 articles underwent comprehensive review and scrutiny in Table 3 post-quality appraisal, ensuring a meticulous and high-impact evaluation process (Ahmad Shazli et al., 2023).

Table 3. Critical appraisal skills program (CASP) checklist

		Yes			No			Total agreement (%)	Comments
		Expert			Expert				
		1	2	3	1	2	3		
Section A: Are the results valid?	1. Was there a clear statement of the aims of the research?	/	/	/				100	Excellent
	2. Is a qualitative, quantitative and mixed-method research approach appropriate?	/	/	/				100	Excellent
	3. Was the research design appropriate to address the aims of the research?	/	/	/				100	Excellent
	4. Was the recruitment strategy appropriate to the aims of the research?	/	/	/				100	Excellent
	5. Was the data collected in a way that addressed the research issue?	/	/	/				100	Excellent
Section B: What are the results	6. Was the data analysis sufficiently rigorous?	/	/	/				100	Excellent
	7. Is there a clear statement of findings?	/	/	/				100	Excellent
Section C: How valuable is the research?	8. How valuable is the research?	/	/	/				100	Excellent

3. RESULTS AND DISCUSSION

This research curated 18 articles through an advanced search methodology strategically chosen to address the research questions. The outcomes of this study are comprehensively presented in Tables 4, 5, and 6, unveiling insights across three distinct themes: (1) the biological activities of *Aquilaria* and sesquiterpenoids, where studies highlight immune-enhancing properties, cytotoxic effects, and potential therapeutic applications; (2) the chemical characterization of *Aquilaria* oil, providing detailed analysis of its composition, quality evaluation, and identification of key bioactive compounds; and (3) the ethnobotanical and medicinal dimensions of *Aquilaria*, documenting traditional uses, pharmacological benefits, and the integration of modern scientific approaches to validate and expand its medicinal potential. These findings collectively underscore the significance of *Aquilaria* in various scientific and medicinal contexts, offering a comprehensive understanding of its diverse applications.

Theme 1: Biological activities of *Aquilaria* and sesquiter-penoids. This facet of the study delves into the intricate biological activities associated with *Aquilaria*, with a particular focus on sesquiterpenoids. The articles selected provide a nuanced understanding of the biochemical and pharmacological properties exhibited by *Aquilaria* and its sesquiterpenoid compounds. From antimicrobial effects to potential therapeutic applications, this theme unveils the multifaceted nature of the biological interactions within the *Aquilaria* genus.

Table 4. Biological activities of *Aquilaria* and sesquiterpenoids

Author	Title	Journal	Objectives	Methodologies	Findings and advantages
Ji, S. Y.; Lee, H.; Hwangbo, H.; Kim, M. Y.; Kim, D. H.; Park, B. S.; Koo, Y. T.; Kim, J. S.; Lee, K. W.; Ko, J. C.; Kim, G.-Y.; Bang, E.; Choi, Y. H. (Ji et al., 2023)	Agarwood pill enhances immune function in cyclophosphamide-induced immunosuppressed mice	Biotechnology and Bioprocess Engineering	Evaluate the potential of AP as an immune function enhancer	BALB/c male mice administered with AP after cyclophosphamide injection	AP supplementation improved spleen index, body weight, and immune cell activity
Zohmachhuana, A.; Malsawmdawngliana; Lalnunmawia, F.; Mathipi, V.; Lalrinzuali, K.; Kumar, N. S. (Zohmachhuana et al., 2022)	*Curcuma aeruginosa* Roxb. exhibits cytotoxicity in A-549 and HeLa cells by inducing apoptosis through caspase-dependent pathways	Biomedicine & Pharmacotherapy	Examine phytochemical content, antioxidant, and anticancer activities of *Curcuma aeruginosa* Roxb.	Sequential extraction of hexane, ethyl acetate, and methanol extracts; cytotoxicity and mode of action assessment	Methanol extracts induced DNA damage and apoptosis in cancer cells
Rhimi, W.; Mohammed, M. A.; Zarea, A. A. K.; Greco, G.; Tempesta, M.; Otranto, D.; Cafarchia, C. (Rhimi et al., 2022)	Antifungal, antioxidant and antibiofilm activities of essential oils of *Cymbopogon* spp.	Antibiotics	Investigate the compositions and biological activities of essential oils from *Cymbopogon citratus* and *Cymbopogon proximus*	GC-MS analysis of Eos; evaluation of antifungal, antibiofilm, and antioxidant activities	Both Eos exhibited antifungal, antibiofilm, and antioxidant activities
Nahar, J.; Boopathi, V.; Rupa, E. J.; Awais, M.; Valappil, A. K.; Morshed, M. N.; Murugesan, M.; Akter, R.; Yang, D. U.; Mathiyalagan, R.; Yang, D. C.; Jung, S.-K. (Nahar et al., 2023)	Protective effects of *Aquilaria agallocha* and *A. malaccensis* edible plant extracts against lung cancer, inflammation, and oxidative stress—*In silico* and *in vitro* study	Applied Sciences	Compare grafted Kynam agarwood (GKA) and normal agarwood for medicinal use	Evaluation of traits, physicochemical indicators, key component groups, and global compositional profile	GKA showed similarities in traits but significant differences in resin content and composition of key component groups
Ning, R.; Mu, H.; Chen, L.; Wang, T.; Xu, X.; He, S.; Jiang, M.; Zhao, W. (Ning et al., 2022)	First report on inhibitory effect against osteoclastogenesis of dihydro-β-agarofuran-type sesquiterpenoids	Journal of Agricultural and Food Chemistry	Quantify agarotetrol in crude drug products containing agarwood	High-performance liquid chromatography analysis	Successful detection and quantification of agarotetrol in various crude drug products

Theme 2: Chemical characterization of *Aquilaria* oil and sesquiterpenoids. The chemical composition of *Aquilaria* oil is explored in-depth in this section. Through the meticulous examination of the selected articles, the study elucidates the diverse compounds present in *Aquilaria* oil, highlighting their concentrations, variations, and potential implications. From essential oils to specific chemical constituents, this theme contributes valuable insights into the chemical complexity of *Aquilaria* oil, fostering a comprehensive understanding of its properties.

Table 5. Chemical characterization of *Aquilaria* oil

Author	Title	Journal	Objectives	Methodologies	Findings and advantages
Lin, Y.; Feng, T.; Dai, J.; Liu, Q.; Cai, Y.; Kuang, J.; Wang, Z.; Gao, X.; Liu, S.; Zhu, S. (Lin et al., 2023)	DNA barcoding identification of IUCN Red listed threatened species in the genus *Aquilaria* (Thymelaeaceae) using machine learning approaches	Phytochemistry Letters	Establish a DNA barcode reference dataset for *Aquilaria* species	Collection of sequences from GenBank and samples; comparison of machine learning approaches	BLOG and SMO effectively identified *Aquilaria* species using specific barcode combinations
Takamatsu, S.; Ito, M. (Takamatsu & Ito, 2022)	Agarotetrol as an index for evaluating agarwood in crude drug products	Journal of Natural Medicines	Detect and quantify agarotetrol in crude drug products containing agarwood	Analysis of crude drug products; establishment of HPLC conditions	Agarotetrol detected and quantified, indicating its usefulness for quality evaluation
Chen, F.; Huang, Y.; Luo, L.; Wang, Q.; Huang, N.; Zhang, Z.; Li, Z. (Chen et al., 2023)	Comprehensive comparisons between grafted Kynam agarwood and normal agarwood on traits, composition, and *in vitro* activation of AMPK	Molecules	Establish a DNA barcode reference dataset for endangered *Aquilaria* species	Collection of authentic sequences, comparison of machine learning approaches and classical methods	Successful identification of *Aquilaria* species using specific barcode combinations
Liu, S.; Wang, J.; Ma, Y.; Cao, X.; Zhang, W.-D.; Li, A. (Liu et al., 2022)	Construction of alkyl-substituted 7-norbornenones through Diels-Alder cycloaddition of electron-deficient olefins and a cyclopentadienone derivative generated *in situ*	Chinese Chemical Letters	Evaluate cytotoxicity and anti-inflammatory properties of *Aquilaria agallocha* and *A. malaccensis*	*In Vitro* assays, in silico evaluation, molecular dynamics simulations	Significant cytotoxicity against A549 cancer cells, anti-inflammatory effects observed
Qiu, Y.; Lai, W.; Feng, Y.; Zhu, Q.; Wang, Y.; Jiang, L.; Lei, F.; Shen, L.; Wu, A. (Qiu et al., 2023)	DFT, FMO, ESP, molecular docking and molecular dynamics simulations of bis-2-(2-phenethyl) chromone as a potential PPAR agonist	Letters in Organic Chemistry	Identify and evaluate dihydro-beta-agarofuran-type sesquiterpenoids	Spectroscopic analysis, X-ray crystallography, ECD calculations	Compounds 4, 6, and 7 from *Celastrus monospermus* Roxb. Inhibit osteoclastogenesis

Theme 3: Ethnobotanical and medicinal insights of *Aquilaria* and sesquiterpenoids. Unveiling the medicinal significance of *Aquilaria*, this theme synthesizes information from the selected articles to provide a holistic view of the plant's ethnobotanical applications and medicinal properties. From traditional uses in indigenous communities to contemporary medicinal perspectives, this section explores the rich tapestry of *Aquilaria's* contributions, positioning it within the broader context of ethnobotany and medicinal research.

Table 6. Ethnobotanical and medicinal insights of *Aquilaria*

Author	Title	Journal	Objectives	Methodologies	Findings and advantages
Hein, P. P.; Arunachalam, K.; Fu, Y.; Zaw, M.; Yang, Y.; Yang, X. (Hein et al., 2023)	Diversity of medicinal plants and their therapeutic usages of Kachin people (Jinghpaw) in the central part of Kachin State, Myanmar	Journal of Ethnopharmacology	Document traditional medicinal plants used by the Kachin people in Myanmar	Interviews with 82 informants from eight villages; classification of reported ailments	117 medicinal plant species recorded, 22 newly identified for Myanmar, Fabaceae and *Lamiaceae* most represented families
Bouhaous, L.; Miara, M. D.; Bendif, H.; Souilah, N. (Bouhaous et al., 2022)	Medicinal plants used by patients to fight cancer in northwestern Algeria	Bulletin Du Cancer	Document medicinal plants used by cancer patients in northwest Algeria	Ethnobotanical surveys with 211 cancer patients; calculation of ICF	53 medicinal plants identified for cancer treatment, including new uses for known plants
Wang, D.; Dong, X.; Nie, Y.; Yang, W.; Li, C. (Wang et al., 2022)	A review on medical plants of genus *Siegesbeckia:* Phytochemical and pharmacological studies	Records of Natural Products	Investigate the pharmacological properties of Genus *Siegesbeckia*	Modern pharmacological research	250 compounds identified, therapeutic activities include anti-inflammation, analgesia, and anticancer
Sundara Rajoo, K.; Lepun, P.; Alan, R.; Singh Karam, D.; Abdu, A.; Rosli, Z.; Izani, N.; James Gerusu, G. (Sundara Rajoo et al., 2023)	Ethnobotanical study of medicinal plants used by the Kenyah community of Borneo	Journal of Ethnopharmacology	Document ethnomedicinal knowledge of the Kenyah community in Sarawak	Repeated interviews, field surveys	Identification of 61 plant species, with some used for treatments scarcely reported in past literature
Krishnan, N.; Singh, P. K.; Sakthivelu, M.; Velusamy, P.; Gopinath, S. C. B.; Raman, P. (Krishnan et al., 2024)	Influence of thermal treatment on extraction and characteristics of phytochemicals from rhizome of *Acorus calamus* L.	Biomass Conversion and Biorefinery	Document traditional medicinal plants used by the Kachin people	Interviews with 82 informants, classification of reported ailments	Recorded 117 medicinal plant species, 22 newly recorded for Myanmar
Dudek, K.; Pietryja, M. J.; Kurkiewicz, S.; Kurkiewicz, M.; Błońska-Fajfrowska, B.; Wilczyński, S.; Dzierżęga-Lęcznar, A. (Dudek et al., 2022)	Influence of the drying method on the volatile component profile of *Hypericum perforatum* Herb: A HS-SPME-GC/MS study	Processes	Develop a one-pot protocol for constructing alkyl-substituted 7-norbornenones	One-pot protocol using electron-deficient olefins and cyclopentenone derivative	Successful construction of sterically congested 7-norbornenone-containing polycyclic compounds
Toh, S. C.; Lihan, S.; Bunya, S. R.; Leong, S. S. (Toh et al., 2023)	*In vitro* antimicrobial efficacy of *Cassia alata* Linn. leaves, stem, and root extracts against cellulitis causative agent *Staphylococcus aureus*	BMC Complementary Medicine and Therapies	Document medicinal plants used by cancer patients in northwest Algeria	Ethnobotanical surveys with 211 cancer patients	Identified 53 medicinal plants used against various types of cancer
Poursaleh, Z.; Vahedi, E.; Movahhed, M.; Ahmadian-Attari, M. M.; Jafari, M.; Kashani, L. M. T.; Khodadoost, M.; Sahebkar, A. (Poursaleh et al., 2022)	Sedative effects of a traditional polyherbal formulation (Monavvem) in patients with chronic insomnia: A randomized double-blind placebo-controlled trial	European Journal of Integrative Medicine	Evaluate sleep quality of chronic insomnia patients using the oral polyherbal formulation "Monavvem"	Randomized controlled trial with Monavvem vs. placebo; ISI and PSQI questionnaires	Monavvem significantly improved insomnia symptoms compared to placebo

4. CONCLUSION

This study highlights the significant biological activities and chemical characterization of *Aquilaria* and sesquiterpenoids, drawing from diverse research articles. Ji et al. (2023) demonstrated the immune-enhancing potential of Agarwood Pill (AP) in cyclophosphamide-induced immunosuppressed mice. Meanwhile, Zohmachhuana et al. (2022) showed the cytotoxic effects and apoptosis induction in cancer cells by sequential extraction of *Aquilaria* extracts. Rhimi et al. (2022) explored the antifungal, antibiofilm, and antioxidant activities of *Aquilaria* essential oils. Meanwhile, Chen et al. (2023) provided insights into the medicinal differences between grafted kynam agarwood and normal agarwood. Takamatsu and Ito (2022) identified agarotetrol's potential in managing osteoclastogenesis, enhancing our understanding of sesquiterpenoids' therapeutic effects. Lin et al. (2023) established a DNA barcode reference for *Aquilaria* species and highlighted the importance of agarotetrol in the quality evaluation of agarwood products. Additionally, Nahar et al. (2023) and Ning et al. (2022) identified cytotoxic and anti-inflammatory properties, as well as PPAR agonists among dihydro-beta-agarofuran-type sesquiterpenoids.

Therefore, future research should investigate the therapeutic potential of identified compounds in clinical settings, conduct further studies on the pharmacological properties and applications of different *Aquilaria* variants, and develop sustainable methods for agarwood production and extraction to preserve natural resources.

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