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Rapid Method for Microencapsulation of *Magnolia officinalis* Oil and Its Medical Applications

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ABSTRACT

Magnolia officinalis, a tree known for its bark, leaves, and flowers, contains phytochemicals that have garnered significant attention in recent research. Modern medicine increasingly incorporates plant extracts, rich in various classes of phytochemicals, either as replacements for traditional treatments or as complementary additions to enhance efficacy and minimize side effects. This study focuses on the extraction of oil from the leaves of *M. officinalis*, which was analyzed using GC-MS, revealing a predominance of monoterpenes (notably linalool and its derivatives) and sesquiterpenes (such as caryophyllene). These compounds are investigated for their potential therapeutic effects across a range of conditions, with a particular emphasis on their mechanisms of action. In addition to chemical analysis, the leaves were examined macroscopically and microscopically. The antimicrobial properties of the extracted oil were tested against both gram-positive and gram-negative bacteria. To address the challenges of oil degradation over time and its limited bioavailability when taken orally, the oil was encapsulated using the coacervation method, a quick and cost-effective technique. The encapsulation protects the oil's properties and improves its bioavailability. Future research will focus on evaluating the bioavailability of the encapsulated oil through oral administration and monitoring its stability during storage.

Keywords: Microcapsules, *Magnolia officinalis*, Medical application, Oil

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Introduction

Magnolia species, which have been cultivated in regions like China, Korea, and Japan for centuries, have gained increasing global attention, including in Europe [1-3]. With approximately 200 magnolia species, extracts from different parts of the tree have been utilized in traditional medicine for treating various conditions such as digestive, respiratory, cardiovascular, bone, and neurological issues (e.g., anti-stress, anti-anxiety, antidepressant), along with antioxidant, anti-inflammatory, anticancer, and hepatoprotective effects [4-6].

Magnolia officinalis, classified within the Plantae kingdom, Tracheophyta division, Magnoliopsida class, Magnoliales order, Magnoliaceae family, and Magnolia genus, is known for its extensive pharmacological properties. These benefits are attributed to its rich composition of monoterpenes, sesquiterpenes, phenolic compounds, flavonoids, and neolignans like magnolol and honokiol [7, 8]. The plant's chemical profile varies based on the part of the plant studied, influencing its medicinal properties [5]. The bark, flower buds, and leaves are considered especially beneficial for their pharmacological effects [2, 9].

Historically, magnolia bark extracts have been utilized in Chinese and Japanese traditional medicine for thousands of years due to their sedative, antioxidant, anti-inflammatory, antibiotic, and antispasmodic properties. These extracts remain popular in herbal medicine today [10]. Magnolol and honokiol, the primary neolignans in magnolia bark, are key compounds responsible for its therapeutic effects. Their concentration varies depending on the magnolia species, its geographic origin, the specific plant part used, and the extraction process [4, 10].

The bark is rich in phenolic compounds, alkaloids, and essential oils, with magnolol and honokiol being the main active ingredients that exert significant pharmacological effects across the digestive, nervous, cardiovascular, and respiratory systems. Additionally, these compounds offer anti-inflammatory, analgesic, antibacterial, antitumor, and antioxidant benefits [11]. Magnolia flower buds, particularly white ones, are rich in monoterpene hydrocarbons, phenolic acids, aromatic amino acids, and monosaccharides, all of which contribute to the synthesis of isoprene and monoterpene hydrocarbon production. Interestingly, purple flower buds have higher levels of β-myrcene, a key monoterpene hydrocarbon, likely due to varying levels of threonine and organic acids. Magnolia flower buds also contain essential oils with effects similar to those of the bark but are generally weaker in their therapeutic functions. They are commonly used for treating digestive discomfort, bloating, and chest or abdominal heaviness [11]. Magnolia leaves contain essential oils, flavonoids, and polysaccharides, with notable antibacterial, antioxidant, and vasodilatory properties [12, 13]. These oils are composed of monoterpene hydrocarbons, monoterpenoids, sesquiterpenes, and various other terpenoids, with eucalyptol, beta-elemenene, linalool, caryophyllene, camphor, and limonene among the most prevalent [8, 14].

One challenge in utilizing these plant extracts is the effective delivery of their active components, particularly volatile compounds, which can degrade when exposed to environmental factors like heat or humidity or when passing through the digestive system. Thus, research is focused on developing methods that preserve these compounds' efficacy during storage and consumption [15].

This paper highlights the extraction of essential oil from *M. officinalis* leaves, including its composition and antibacterial properties. It also introduces an innovative approach to encapsulating the oil using the coacervation process, which enhances its stability for longer storage and improves its oral administration by masking its strong odor and taste. Additionally, recent literature identifies the main therapeutic applications of this oil.

Materials and Methods

Macroscopic analysis of M. officinalis leaves

The macroscopic examination focuses on evaluating characteristics such as the leaf's external appearance, size, texture, and color, which are observed either directly or with the aid of a magnifying tool. The tactile properties, hardness, and scent are also assessed, along with differences in the upper and lower surfaces of the leaves [16].

Microscopic study of M. officinalis leaves

For microscopic evaluation, a transverse section of the vegetative organ was prepared to identify secretory structures and protective bristles that are unique to the species. The analysis was conducted using an Optika B350 microscope [17].

Extraction of essential oil from M. officinalis leaves

To extract the volatile oil from *M. officinalis* leaves, 50 grams of the plant's aerial parts were dried at 65 °C in an oven until their weight stabilized. After drying, the plant material was pulverized and processed in a Soxhlet extractor using petroleum ether as a solvent. The extraction was conducted at 65 °C for 8 hours. Following this, the solvent was removed using a Heidolph Rotary Evaporator (Laborota 4000) set at 100 rpm for 45 minutes [6, 15, 16].

GC-MS analysis of M. officinalis essential oil

For the GC-MS analysis, 0.100 ml of the essential oil was dissolved in 1 ml of ethanol at a 1:10 dilution. The analysis was carried out using a Thermo GC-MS (Trace 1310 ISQ 7000) fitted with an HP-5MS capillary column. Electron ionization (70 eV) was applied, and helium was used as the carrier gas. A 1 µL sample was injected, with the mass transfer line and injector temperatures set at 220 °C and 290 °C, respectively. The oven temperature began at 45 °C for 1 minute and was then ramped up and maintained at 250 °C for 5 minutes [18].

Antimicrobial activity of M. officinalis oil

The antimicrobial effectiveness of *M. officinalis* oil was tested against several bacterial strains, including gram-positive Staphylococcus aureus ATCC 25923 and gram-negative Pseudomonas aeruginosa ATCC 497757 and *Escherichia coli* ATCC 25922. The Kirby-Bauer disk diffusion method was used to determine antimicrobial activity. Bacterial suspensions were prepared in sterile saline and adjusted to a 0.5 McFarland standard. After inoculating the agar plates, paper discs impregnated with 40 µg of Magnolia oil were placed on them. Ciprofloxacin (5 µg/disc) and gentamicin (10 µg/disc) were used as positive controls. The plates were incubated at 37 °C for 24 hours, and the antimicrobial activity was measured by the inhibition zone diameter [19, 20].

Coacervation method for formulating M. officinalis oil microcapsules

The essential oil of *M. officinalis* was incorporated into microcapsules using a straightforward coacervation technique. This process involved mixing 100 g of balsamic vinegar and 2.5 g of agar-agar, followed by heating the mixture to activate the polymer. Afterward, 2 g of Magnolia oil was added dropwise while stirring. To form the microcapsules, the hot mixture was carefully dropped into cold olive oil (held at 4 °C for 30 minutes). Once the microcapsules had formed, they were separated from the olive oil, washed with distilled water, and dried until they reached a constant weight to enhance their stability during storage **(Figure 1)** [21-23].

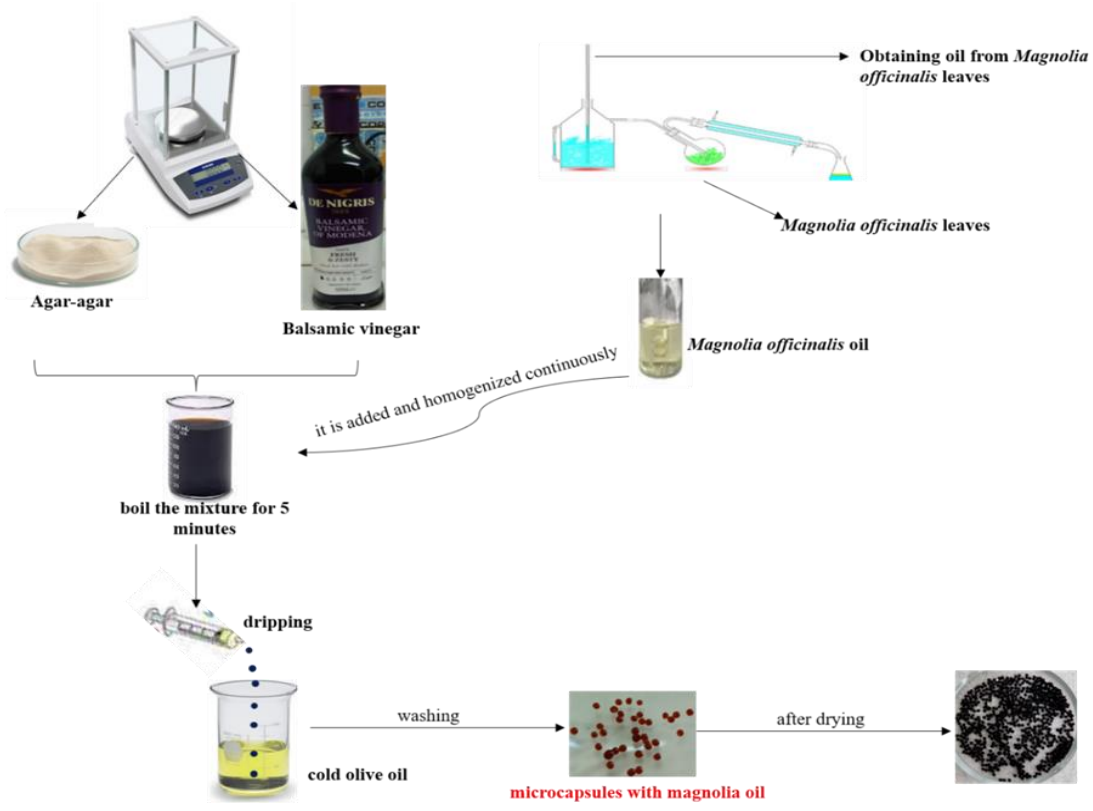


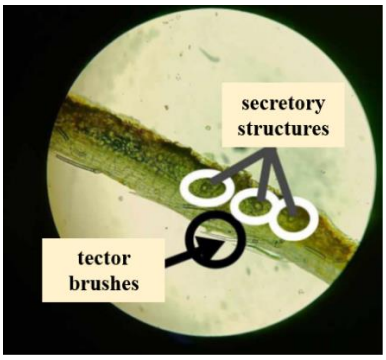
Figure 1. Obtaining microcapsules with *M. officinalis* essential oil.

Results and Discussion

Based on the macroscopic evaluation, the observed organoleptic characteristics were consistent with those reported in previous studies [6, 10, 15]. The leaves exhibit smooth margins, and their coloration can range from

green year-round to deciduous, depending on environmental factors. The leaves typically measure between 12 and 20 centimeters in length and can have a width of up to twelve centimeters.

a) Macroscopic analysis of leaves



b) Transverse section of the leaf

Figure 2. Macroscopic (a) and microscopic (b) analysis of the *M. officinalis* leaf.

The microscopic examination revealed the presence of secretory structures and tectorial bristles in the leaf cross-section. The upper and lower epidermises, along with the assimilative tissue, were also clearly visible. The epidermis is formed by a single layer of large cells, with a thick cuticle coated in wax. Stomatal cells, which are smaller and unevenly thickened, were observed on both sides of the leaf. These stomatal cells are positioned below the epidermal level and are accompanied by accessory cells.

The upper epidermis corresponds to the top side of the leaf, while the lower epidermis is located on the opposite side. The space between these two layers is filled by the core, which contains elongated cells situated perpendicular to the epidermis. These cells are rich in chloroplasts, arranged in chains, and they make up the assimilative tissue, where the leaf's primary functions, such as photosynthesis, are concentrated. The epidermis structure is similar to that of the stem, with stomata covered by tectorial bristles and rarely glandular. Oil is stored in the secretory structures of the leaf.

Extraction and characterization of M. officinalis essential oil by GC-MS

After completing the extraction procedure outlined in section 2.3, a total of 4.6 mL of a yellowish-white volatile oil with a strong, distinct odor was obtained. This oil was stored in a dark, cold environment before gas chromatography-mass spectrometry (GC-MS) analysis. The analysis led to the identification and quantification of various compounds, as summarized in **Table 1** and illustrated in **Figure 2**.

Table 1. The main compounds were identified by GC-MS analysis of the oil obtained from *M. officinalis* leaves.

No.	Denumire substanta	RT (min)	Peaknumber
1.	Acid 2-metil-valeric	7.50	28
2.	3-Thujene	7.56	29
3.	3-Carene	7.73	31
4.	1S-alfa-Pinene	7.81	32
5.	Camphene	8.08	33-34
6.	4-Metilen-1-(1-metiletil)-biciclo(3,1,0)hexan	8.76	36
7.	Beta-Pinene	8.84	37
8.	Beta-Myrcene	9.15	39
9.	O-Cymene	9.98	48
10.	D-Limonen	10.10	49
11.	Eucaliptol	10.17	50
12.	**Cis-Linalool oxide**	11.20	55
13.	**Trans-Linalool oxide**	11.28	56

14.	**Linalool**	11.75-12.54	59-81
15.	Endo-Borneol	13.67	89
16.	**Trans-Linalool 3,7-oxide**	13.78	90
17.	Terpineol	14.21	93
18.	**Caryophyllene**	19.41-19.58	134-140

The analyses revealed that *M. officinalis* essential oil is rich in monoterpenes and monoterpenoids, with linalool being the predominant compound, constituting around 30%. Additional derivatives such as cis-linalool oxide, trans-linalool oxide, and trans-linalool 3,7-oxide were also identified. The peak associated with this compound is shown in **Figure 3**.

Linalool is a widely distributed monoterpene in the essential oils of many plants, including *M. officinalis*. It is an acyclic monoterpene alcohol with a low molecular weight and a hydroxyl group, which imparts polarity and contributes to its biological activity [15]. Linalool has demonstrated antioxidant, anti-inflammatory, antitumor, and antibacterial effects, notably against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* [15, 24].

This compound is a naturally occurring terpene alcohol found in various plant species and is well known for its aromatic properties. Linalool is a colorless oil classified as an open-chain monoterpenoid. It is also recognized as a metabolite and antibacterial agent in plants, along with its widespread use in commercial applications due to its pleasant scent [25].

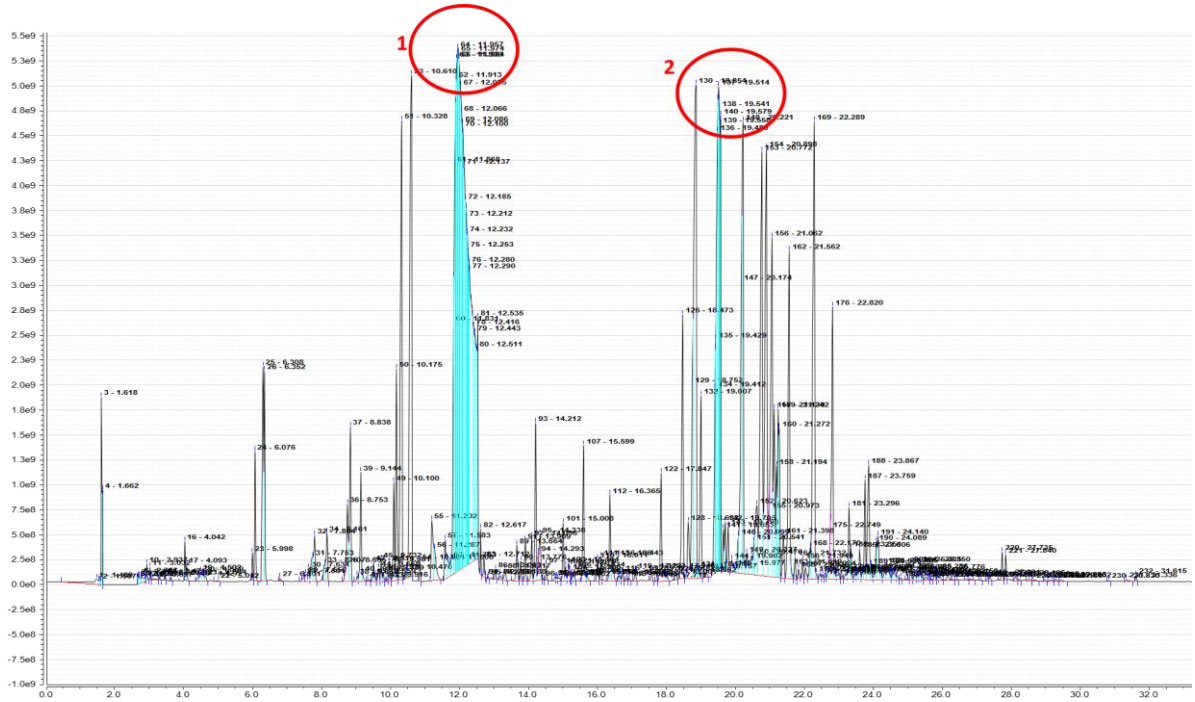


Figure 3. Chromatogram of *M. officinalis* essential oil.

The compound indicated by peak number 2 in **Figure 3** is Caryophyllene, a major component present at 25%. This compound falls within the sesquiterpene class and has a bicyclic structure. Caryophyllene is widely recognized in the literature for its anti-inflammatory effects and strong anticancer properties. Additionally, it is noted for its antioxidant activity, where it prevents the formation of reactive oxygen species, and it also exhibits re-epithelializing effects [26].

Antimicrobial activity testing of M. officinalis oil

To test the antimicrobial properties of *M. officinalis* oil, Ciprofloxacin (5 micrograms) and Gentamicin (10 micrograms) were used as reference standards. The *M. officinalis* oil was applied in a volume of 40 µl, and the inhibition zones were measured for each sample, as depicted in **Figure 4**.

	Staphylococcus aureus	***Escherichia coli***
	Inhibition diameter (mm)	
Magnolia oil 40 µl	13	11
Ciprofloxacin 5 µg	27	30
Gentamicin 10 µg	24	20

Figure 4. The results of testing the antimicrobial activity of *M. officinalis* oil compared to two known antibiotics, using the diffusion method.

Figure 4 demonstrates the most notable antibacterial response in Staphylococcus aureus, with an inhibition zone measuring 13 mm. This result is largely due to the presence of linalool, a compound prevalent in the *M. officinalis* oil, known for its antimicrobial properties [15]. Literature has also documented the efficacy of linalool against pathogens like *Candida albicans*, *Aspergillus brasiliensis*, *Porphyromonas gingivalis*, *Prevotella nigrescens*, *Aggregatibacter actinomycetemcomitans*, and *Streptococcus sobrinus*. Additionally, linalool has been reported by Duarte *et al*. to inhibit *Campylobacter jejuni* and *Campylobacter coli* strains.

Incorporation of M. officinalis oil in microcapsule formulation

M. officinalis oil, rich in bioactive compounds such as linalool and caryophyllene, is characterized by poor solubility and bioavailability in conventional formulations. To address this, integrating the oil into various transport systems—such as liposomes, nanocapsules, and microcapsules—improves its bioavailability and extends the shelf life, providing a protective barrier against environmental factors that may cause degradation [27]. Previous studies have explored the use of cyclodextrins to enhance oral bioavailability, polybutylcyanoacrylate nanocapsules for prolonged storage stability, and lipid-based nanoparticles for enhanced absorption through the skin [15].

In this study, we employed the coacervation method to encapsulate *M. officinalis* oil, a technique that is both inexpensive and uses biocompatible materials. An advantage of this method is its rapid execution time—approximately 30 minutes. **Figures 5a and 5b** show the microcapsules created by this process. The initial microcapsules before drying, as depicted in **Figure 5a**, retain a spherical shape and the coloration from the formulation materials, whereas after drying, the capsules take on a more irregular form due to the dehydration process, as shown in **Figure 5b**.

a) b)

Figure 5. Microcapsules with *M. officinalis* oil before (a) and after drying (b).

After the encapsulation and subsequent drying of *M. officinalis* oil, the oil demonstrated enhanced preservation, effectively shielding it from environmental factors like light, temperature, and humidity. This improved stability

is expected to be advantageous in future studies, where the effects of the oil will be examined through oral and topical administration.

Therapeutic uses of M. officinalis oil

In this section, the therapeutic potential of the primary compounds identified in the GC-MS analysis—namely linalool, linalool derivatives, and caryophyllene—is explored in terms of their medicinal properties. These compounds exhibit a wide range of therapeutic effects, supported by both in vitro and in vivo evidence [15, 28, 29].

Antioxidant and antimicrobial properties

Research shows that extracts from various Magnolia species, including *M. officinalis*, possess significant antioxidant properties. These are typically assessed using methods such as FRAP, CUPRAC, and DPPH, which confirm their ability to neutralize free radicals in the body and prevent oxidative damage, potentially reducing the risk of cancer. Regarding antimicrobial activity, *M. officinalis* oil has demonstrated efficacy against both gram-positive and gram-negative bacteria, such as Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus, as well as antifungal effects against Candida albicans, as noted by Pereira *et al*. [15].

Anti-inflammatory effects

Linalool and its derivatives play a critical role in modulating inflammation by inhibiting key inflammatory markers such as TNF-α and interleukin-6 (IL-6) [30, 31]. In vitro studies reveal that linalool can block the NF-kB and MAPK signaling pathways, both of which are involved in inflammatory responses. Animal models of lung inflammation have also shown that linalool and related compounds effectively suppress inflammatory cytokines such as TNF-α, IL-6, and IL-1β. Additionally, linalool has been found to reduce the production of nitric oxide, further aiding in the reduction of inflammation [32].

Anticancer properties

The anticancer potential of linalool and caryophyllene lies in their ability to inhibit the proliferation and differentiation of malignant cells, inducing apoptosis in cancerous cells [33]. Furthermore, their strong antioxidant capabilities help neutralize reactive oxygen species, acting as preventive agents against the onset of cancer. Cheng *et al*. [34] demonstrated that linalool achieves this effect primarily by inhibiting superoxide dismutase 2 activity, a key enzyme involved in the management of oxidative stress. In vitro studies have confirmed that linalool and similar monoterpenes selectively target cancer cells, such as those from breast, prostate, cervical, leukemia, and colon cancers, inducing cell death while sparing healthy cells [35].

Antihyperlipidemic and antiobesity effects

Linalool has shown promise in lowering lipid levels in the body, exerting anticholesterolemic and antiatherosclerotic effects, thus protecting cardiovascular health. Caryophyllene, on the other hand, has been found to combat obesity, fatty liver disease, and related cardiovascular issues, acting through cannabinoid receptors (CB2) and influencing peroxisomal activity [15, 36].

Antinociceptive effects

Studies exploring the antinociceptive effects of linalool have largely focused on animal models. Kuwahata *et al*. [37] demonstrated that linalool, both alone and in combination with other pain-relief agents, increased nociceptive activity, suggesting its potential as an effective pain management option. The proposed mechanism involves the reduction of spinal extracellular signal-regulated protein kinase activation. As such, linalool may be useful either independently or in conjunction with other therapies for treating acute or chronic pain conditions, including carpal tunnel syndrome [38, 39].

Antidepressant and anxiolytic effects

The antidepressant and anxiolytic effects of *M. officinalis* oil are attributed to its high linalool content, which acts on sodium channels in neurons and interacts with serotonin A1 receptors and α2 adrenergic receptors [40, 41]. According to Cheng *et al*. [34], linalool administration leads to a decrease in dopamine, serotonin, and norepinephrine levels, which contributes to its mood-stabilizing effects.

Conclusion

In summary, this study emphasizes the medicinal potential of compounds present in *M. officinalis* oil, particularly focusing on its antimicrobial properties. The essential oil was extracted from the leaves of the plant, and both macroscopic and microscopic analyses were conducted to identify the botanical characteristics of the species. The chemical profile of the oil was analyzed using GC-MS, revealing that the predominant compounds, making up 30% of the oil, were monoterpenes, primarily linalool and its derivatives, while sesquiterpenes, particularly caryophyllene, accounted for approximately 25%. The oil demonstrated significant antimicrobial activity against both gram-positive and gram-negative bacteria. Given that the oil's properties degrade during storage and along the digestive tract during oral administration, it is necessary to encapsulate it in controlled delivery systems, such as microcapsules. Microcapsules containing the oil were successfully formulated using biocompatible, cost-effective materials via a rapid coacervation method. These capsules retained a spherical shape initially, which transformed into an irregular form post-dehydration. This encapsulation effectively masked the strong flavor and odor of the oil, while also enhancing its stability and preserving its therapeutic properties.
Looking ahead, future research will focus on evaluating the long-term stability of the capsules and conducting in vitro studies on controlled release in simulated gastrointestinal fluids, aiming to develop a controlled-release system for oral administration.

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Ethics Statement: None

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