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#### **Review Article**

# An update and comprehensive review of the plant extracts and essential oils as a potential treatment for bacterial mastitis in dairy cattle

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#### Abstract

Bovine mastitis is the most common disease caused by bacteria, viruses, fungi, and chemicals in dairy herds, causing economic loss and food safety concerns. The treatment and prevention of this disease are primarily through antimicrobial agents. Still, antimicrobial resistance could hamper the effectiveness of conventional drugs for this disease. Furthermore, antimicrobial residues in milk and the environment may endanger human health. This shows that using plants and essential oils (EOs) to prevent mastitis in cattle might be feasible. Several plants are known to possess antimicrobial properties, and plant extracts and EOs are generally considered safe for animals, humans, and the environment. This review article summarizes the ongoing issues encountered in the classical treatment of mastitis and the impact of the most common plant extracts and EOs on bovine mastitis as an alternative method of controlling these pathogens, as well as the drawbacks of using these plant derivatives. Finally, plant extracts and EOs have good antibacterial activity against bacteria isolated from bovine mastitis milk. However, the use of these plant extracts and EOs as medicines requires numerous clinical trials on dairy farms.

Keywords: Essential oils, Plant extract, Bacterial mastitis, Dairy cattle

#### Introduction

Despite years of study, mastitis remains the most economically destructive and potentially zoonotic disease for the dairy industry and consumers, caused by a variety of organisms and significantly impacts milk quality (Cheng and Han, 2020; Maity and Ambatipudi, 2021). The highest risk of contracting a disease common to humans and animals is when

consuming raw milk (Maity and Ambatipudi, 2021). Mastitis costs include direct and indirect costs such as discarding milk, reduced milk production, reduced reproduction, and premature culling and replacement (Griffioen et al., 2016). Mastitis can be classified into two clinical and subclinical groups. The symptoms that are visible with clinical mastitis include milk clots, hardness, and

swelling in the teat. However, external changes are not visible in subclinical mastitis (SCM), and the diagnosis is made by counting somatic cells or by means of the California mastitis test (CMT) (Sadek et al., 2016; Lopesa et al., 2020).

The causes of mastitis can be categorized as environmental or contagious factors. Environment-related agents penetrate the cow's udder through the teat canal or via passive penetration soon after milking but contagious pathogens are transmitted from one cow to another (Lopesa et al., 2020). The contagious pathogens include Staphylococcus aureus (S. aureus), Streptococcus galactic, Streptococcus dysgalactiae, Mycoplasma spp., and Corynebacterium bovis, while environmental agents fall into Streptococcus uberis (S. uberis), Streptococcus faecalis, Citrobacter Enterobacter spp., Escherichia coli (E. coli), Klebsiella spp, and Pasteurella spp. (Lopesa et al., 2020). E. coli causes mild to severe clinical mastitis, and there are clear signs of inflammation in the affected gland (Lavon et al., 2019). It has been reported that E. coli O157:H7 can produce Shiga toxin. This toxin has been identified as a possible agent of human transmission via direct contact and the dairy farm environment (Murinda et al., 2019). Furthermore, S. aureus is often considered to be the most important bacterial zoonotic agent, infecting humans and a variety of wild animals, particularly dairy cattle (Peton and Le Loir, 2014; Algharib et al., 2020). S. uberis is one of the most significant pathogens of bovine mastitis, causing subclinical and clinical mastitis in and non-lactating cows both lactating (Montironi. 2016). Both clinical subclinical mastitis is caused by Enterococcus spp., Enterobacteriaceae spp., Bacillus spp., S. chromogenes, Corynebacterium Microbacterium spp., and Kocuria spp. (Ashker et al., 2015). These pathogens and their related toxins induce a set of pathogenesis mechanisms involving

inflammation, immune and oxidative disturbance, and septicemia, which ultimately leads to tissue and morphological changes in tissue along with biochemical, microbiological, and physical changes in milk (Ezzat Alnakip et al., 2014). Many natural products with antibacterial, antifungal, and antiprotozoal properties that can be used systemically or locally. With the emergence of drug-resistant bacterial strains and the adverse effects of antibiotics and other drug residues in milk, there is a need to choose alternative measures to control bovine mastitis (Reverter et al., 2014). Herbal medicines are emerging as the main source of alternative treatments for important mammalian diseases in the current era of emerging antibiotic resistance due to their potent pharmacological activities, low toxicity, and economic viability (Atef et al., 2019).

Plant extracts exert differential antimicrobial, anti-inflammatory, immunomodulatory, and antioxidant effects against different bacterial species (Atef et al., 2019). It is possible to use certain plants therapeutically. The chemical compounds present in these plants have been shown to have biological properties that may be beneficial to human and animal health (Paz et al., 2018). The use of medicinal plants has led to recent empirical observations that have fueled research into these bioactive substances and the potential for new product development.

An essential oil (EO) is an aromatic and volatile liquid extract and the byproduct of plant metabolism. It is a defense mechanism against pathogens that are considered a substance with significant antimicrobial **EOs** activity. Some are continuously produced, but others are produced in response to microbial infection or tissue damage (to prevent microbial entry) (Hanif et al., 2018). According to the International Organization for Standardization (ISO), EOs are products obtained by steam distillation from a plant's raw material, mechanical processes from

citrus rinds, or distillation following the separation of aqueous phases by physical methods (Gupta et al., 2020). In medicine, these oils are used as anti-inflammatory agents, wound healers, relaxants, antibacterial, immune boosters, and digestive aids (Manion and Widder, 2017). The present paper aims to review the effects of plant extracts and EOs against bovine mastitis and their use as an alternative and complementary treatment, given their properties for use in this area.

#### Materials and methods

We selected and analyzed the articles related to the effect of plant extracts and EOs on bovine mastitis between 2010 and 2022 through searches on Google Scholar, Science Direct, the National Library of Medicine (PubMed), and Springer Link.

# **Bovine Mastitis: Common Treatment and Bacterial Resistance**

The most common treatment method is the intramammary infusion of antibacterial agents (Pozzo et al. 2012). Most antimicrobial agents are known for their mechanisms of action, which relate to any number of bacterial targets or processes, including inhibition of protein synthesis, inhibition of metabolic pathways, disruption of cell wall synthesis, inhibition of DNA and RNA synthesis, and the lysis of the bacterium membrane (Chandra et al., 2017). Drugs such as ampicillin, penicillin G, streptomycin, gentamicin, erythromycin, ciprofloxacin, oxytetracycline, doxycycline, trimethoprim/sulfamethoxazole have been used in bovine mastitis and are effective against S. aureus (Ismail, 2017). Antibiotics such as amoxicillin and clavulanic acid, ceftiofur, cephalexin, ciprofloxacin, enrofloxacin. streptomycin, gentamicin, marbofloxacin, neomycin, oxacillin, penicillin, tetracycline, and trimethoprim/sulfamethoxazole have been reported to be effective against bacteria such as Staphylococcus hyicus, S. epidermidis, S.

intermedius, and Corynebacterium spp. isolated from bovine mastitis (Alba et al., 2019).

Regarding the main mechanism of bacterial

resistance to antibacterial agents, we can mention the limitation of drug absorption, altered drug target, receptor inactivation, enzymatic metabolism of antimicrobial agents, biofilm formation, and active drug efflux. These mechanisms may intrinsically related to microorganisms or acquired from other microorganisms (Reygaert et al., 2018; Varela et al., 2021). The mechanisms used by bacteria to become resistant to antibiotics are very varied and depend on conditions. For example, whether they have developed resistant variants, whether they have experienced differential reproductive success under antibiotic treatment, and whether there has been variation in the population (Baquero, 2011). According to Ameen et al. (2019), antibioticresistant mastitis pathogens were predominant in dairy herds, as they discovered that 90% out of 51 strains of S. uberis were highly resistant to penicillin. A large number of S. aureus isolates also showed resistance to tetracycline (57% of the strains) and gentamicin (27%). By contrast, many S. uberis isolates were susceptible to amoxicillin-clavulanic (80%), erythromycin (84%), oxacillin (73%), and trimethoprim/sulfamethoxazole (84%), and 40% of E. coli isolates were resistant to streptomycin (Ameen et al., 2019). Moreover, 33% of isolates were resistant to ampicillin, to trimethoprim-sulphamethoxazole, 20% to ceftriaxone, 16% to cefepime, and 16% to tetracycline (Ameen et al., 2019). High sensitivity was observed for E. coli to certain antibiotics, including amoxicillin and clavulanate, ciprofloxacin, and neomycin. Over 60% of the strains were sensitive to these antibiotics. It has been suspected that milk can be a major source of antimicrobial drugs and resistant microorganisms that enter the food chain (Kromker and Leimbach, 2017). Moreover, 90% of antibiotic residues in milk are the result of mastitis treatment (Kovacevi et al., 2021).

Antibiotic resistance of bacterial strains has increased rapidly, such that current antibiotics may become ineffective within 5 years due to genetic changes (Chandra et al., 2017). For this reason, it is imperative to identify and use alternatives to prevent and treat mastitis in such food-producing species, nanomaterials, bacteriophages (Gomes and Henriques, 2016), and electrical signals 2019). This review (Willmer, briefly discusses EO and plant extracts that are used for the treatment of bovine mastitis caused by bacteria.

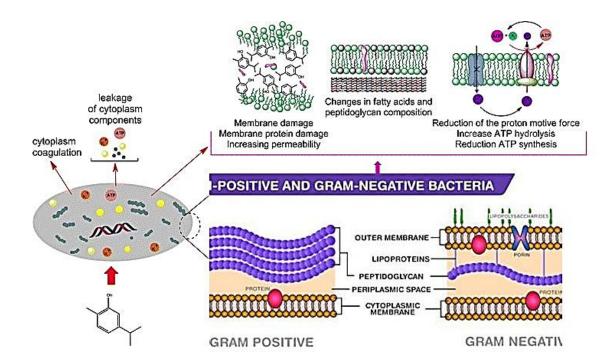
#### Thymus vulgaris

Thymus vulgaris( T. vulgaris) is native to eastern Azerbaijan and southern Europe, from the western Mediterranean to southern Italy. Thymus species of aromatic plants are useful medicinal plants with EOs known as thyme oil which has various therapeutic properties such as B. antimicrobial, cardioprotective, antiseptic, and diuretic effects (Emami Bistgani et al., 2022). A bushy subshrub, T. vulgaris has small, fragrant, grey-green leaves and small purple or pink flowers in early summer and grows well in a sunny spot where there is no shade; it prefers a warm, dry climate. Thyme species thrive best in coarse, rough soil, which may be unsuitable for some alternative crops (Hosseinzadeh et al., 2015). Kovacevi et al. (2021) reviewed T. vulgaris against clinical and subclinical bovine mastitis. They found Streptococcus spp., E. coli, Enterobacter sakazakii, Kelebsiella oxytoca, S.aureus, Streptococcus uberis, and **Streptococcus** dysgalactiae. Among pathogens, E. coli was the most common pathogen identified in six samples (19.35%), followed by five (16.13%) samples with Streptococcus spp., while Staphylococcus spp., coagulase negative, Streptococcus uberis, Streptococcus dysgalactiae, Klebsiella oxytoca, and Enterobacter sakazakii each existed in one sample (3.23%). In their study, EO from T. vulgaris showed more significant antibacterial potential against Streptococcus spp., Entrobacter sakazakii and E. coli (Kovacevi et al., 2021) (Abboud et al., 2015). The mechanism of action of thymol against microorganisms has not been investigated, however, it probably has a mechanism similar to that of carvacrol (Figure The alteration in the cytoplasmic membrane may damage the outer and inner membranes while interfering with membrane function (Chouhan et al., 2017). ATP and K<sup>+</sup> are also released by contacting a membrane, resulting in increased membrane permeability. Amongst various components, only carvacrol, citral, thymol, and trans-cinnamaldehyde (TC) have been effective with lower MIC values against all pathogens such as Streptococcus spp., E. coli, Enterobacter sakazakii, Kelebsiella oxytoca, S.aureus. Streptococcus uberis. and Streptococcus dysgalactiae (Gupta et al., 2020).

A structural study of T. vulgaris has shown that thymol (54.17%) is the most abundant compound followed by y terpinene (22.18%) and p-cymene (16.66%) (Kovacevi et al., 2021). According to the results of Martínez et al. (2021), the most active phytochemicals were terpenes and polyphenols, either alone or in combination with EOs or extracts of plants. Compounds including, isorhamnetin glycoside, luteolin glycoside, hibicuslide C, chryseriol glycosides, and propolin D have been shown to be effective against both Gramnegative (Vibrio cholerae) and Gram-positive (S. aureus) bacteria by disrupting the plasma membrane and leaking intracellular content, similar to or even more effective than ciprofloxacin used as a reference drug (Tagousop et al., 2018). Mullen (2020) Phyto-Mast known studied the commercial product consisting of EOs of Angelica sinensis, Gaultheria procumbens,

Glycyrrhiza uralensis, and T. vulgaris. He found that only T. vulgaris oil had consistent antibacterial activity, and a combination of

oils did not show typical dose-response effects.



**Fig. 1.** Mechanism of Carvacrol on alteration in the cytoplasmic membrane and damage to inner and outer membrane (Marinelli et al., 2018)

#### Minthostachys verticillata

The ethnobotanical aromatic herb, Minthostachys verticillata (Griseb) Epling (Lamiaceae). commonly known "peperina", has a wide range of uses and properties. This species exists in east Azerbaijan (Latifian and Arslanoglu, 2018) as well as in South American countries such as Brazil, Venezuela, Bolivia, Ecuador, and Argentina's northwest and central regions (Montironi et al., 2022). It is used in folk medicine for sedative its antispasmodic, digestive, and stimulant properties, in addition to treating respiratory ailments, including asthma and bronchitis. Several in vitro studies found have that this plant exhibits antibacterial, antiviral. and antifungal properties. According to a study by Cariddi et al. (2011), pulegone (51.7%) and menthone (37.8%) made up the main compounds in M. verticillata oil, along with 1.4% of cismenthone and 1.4% of piperitone. The antibacterial activity of M. verticillata against S. aureus was assessed by Cecchini et al. (2020) after the incubation of S. aureus with various concentrations of EO for 24 h. This study supports the notion that nanoformulations based on natural products are potentially helpful antibacterial agents. In vitro and in experimental mouse models, the effect М. verticillata immunomodulation has been demonstrated in terms of both decreasing pro-inflammatory mediators such as histamine hexosaminidase and increasing proinflammatory cytokines such as IL-10 (Montironi et al., 2019). Additionally, M. verticillata EO has proven to be safe in

experimental animals by using various routes, it does not cause cytogenotoxicity or toxicity to the bone marrow or blood cells (Escobar et al., 2012). Cerioli et al. (2018) assessed the antibacterial activity of M. verticillata EO and limonene against bacteria isolated from bovine mastitis, including E. coli, Bacillus pumilus, and Enterococcus faecium. They used time-kill assays, bacterial minimum inhibitory concentration (MIC), and minimum bacterial concentration (MBC) to perform their analysis. The result from M. verticillata EO indicated an inhibitory effect on all isolates, but limonene inhibited B. pumilus. Results obtained from bacterial lysis revealed that M. verticillata EO was able to produce 50% of bacterial lysis after 30 min while limonene failed to produce bacterial lysis. M. verticillata EO and limonene were studied by Montrioni et al. (2016) for their effectiveness against the S. aureus strains isolated from bovine mastitis. It was observed that the MIC value for M. verticillata EO ranged from 14.3 to 114.5 mg/mL and the MBC value ranged from 114.5 to 229 mg/mL while limonene values ranged from 3.3 to 52.5 mg/mL and the MBC was 210 mg/mL (Table 1). Both compounds had antimicrobial

potential against *S. aureus* strains isolated from bovine mastitis (Table 2).

### Origanum vulgar

Origanum vulgare is one of the species belonging to the Lamiaceae family, which is native to the Mediterranean region and western Eurasia. Origanum vulgare L. subsp. viride also grows in the northern part of Iran (Andi and Maskani, 2021). Various traditional healing systems use this aromatic herb as a remedy and spice around the world (Pezzani et al., 2017). Since ancient times, the Origanum vulgare plant has been used as an herbal medicine for the treatment of dyspepsia, painful menstruation, rheumatoid arthritis. scrofulosis, and urinary tract disorders (Ocaña-Fuentes et al., 2010; Gulluce et al., 2012; Sarikurkcu et al., 2015;). Previous studies showed that intermammary treatment with oregano essential oil reduced bovine mastitis with S. aureus and E. coli compared to gentamicin (Cho et al., 2015). The results showed that this extract can be a useful alternative to antibiotics in controlling mastitis (Table 2). Several phenolic compounds are in Origanum, such as carvacrol and thymol, making it an effective antibacterial. The primary mechanism by which carvacrol acts on bacteria is through the breakdown of the proton driving force, leading to the depletion of the ATP pool and cell death (Thormar, 2010).

Table 1. MIC and MBC of different plant extracts and essential oil

Essential oil	MIC*	MBC *	REFERECCE
Thymus vulgaris	0.8-3.2mg/mL	1.6-3.2mg/ml	Dal pozzo et al. (2011)
Minthostachys verticillata	14.3-114.5mg/ml	114.5-229mg/ml	Montironi et al. (2016)
Limonene	3.2-52.5mg/ml	210mg/ml	Montironi et al. (2016)
Origanum vulgare	0.62-1.86mg/ml	1.25-2.75mg/ml	Renu gupta et al. (2020)
Cinnamomum zeylanicum	1.6-6.4mg/ml	1.6-6.4mg/ml	Renu gupta et al. (2020)
Thymol	0.2 - 0.8  mg/ml	0.4-6.2mg/ml	Dal pozzo et al. (2012)
Carvacrol	0.2 - 1.6 mg/ml	0.2 - 3.2 mg/ml	Dal pozzo et al. (2012)

<sup>\*</sup>Minimum inhibitory concentration (MIC)

#### Rosemary

It is a widely used medicinal plant (Rosmarinus officinalis) belonging to Lamiaceae family. *Rosemary* officinal leaves

are commonly used in traditional Mediterranean cuisine and folk medicine (Ribeiro-Santos et al., 2015). *Rosemary* EO and preparations contain antibacterial,

<sup>\*</sup>Minimum bactericidal concentration (MBC)

cytostatic, antimutagenic, antioxidant, and anti-inflammatory properties (Milyuhina et al., 2020). Research has shown that rosmarinic acid (RA) reduces tissue damage in some inflammatory diseases, such as acute lung injury, inflammation development, genesis (Jiang et al., 2017). 1,8-cineole, the main compound of rosemary leaf EOs, has been shown to have significant antibacterial properties against numerous microorganisms such as E. coli, S. aureus, Bacillus subtilis, and Bacillus cereus (Milyuhina et al., 2020). The anti-inflammatory effects of RA on the inflammation caused by lipopolysaccharide (LPS) in the epithelial cells of mouse mammary tissue have been reported (Jiang et al., 2017). After treatment with RA, they observed significantly improved structural damage to the breast and decreased myeloperoxidase activity. Using the results obtained by qPCR and ELISA, they found that the expression of TNFα, IL-1, and IL-6 decreased in a dose-dependent manner in both tissues and mMECs. Additionally, RA was found to suppress the protein levels of TRAF6, TLR4, IRAKA, MyD88, and p-IKKB. Moreover, RA inhibited the activation of the NF-kB signal transduction pathway by LPS. In conclusion, RA inhabits the NF-kB, MyD88, and TLR4 signaling pathways to attenuate LPS-induced mastitis in dairy cattle.

**Table 2.** The activity of some essential oils (EOs) and plant extracts against bacteria that cause dairy cattle mastitis.

Plant /Essential oil	Microorganism	Result	References
Origanum vulgare	Staphylococcus aureus	A 0.9 ml EO administered twice daily for 3 days into inflamed quarters resulted in decreased WBC and SCC 16 and no detectable <i>Streptococcus aureus</i> Or <i>E. coli</i> in the milk on the fourth post-treatment day.	Cho et al., 2015
Rosemary EO Cinnamon EO Geranium EO	Candida albicans	showed highly antibacterial activity against the Candida albicans, with values ranging from 15 to31 g/ml	ksourii et al., 2017
Thyme EO Lavender	Staphylococcus spp Streptococcus spp	External use of these oils in Vaseline resulted in a greater antibacterial action against the <i>Staphylococcus spp and Streptococcus spp</i> for a 100% recovery rate with thymus EO	Abboud et al., 2015
M. verticillata EO	E. coli, Entrobacter faecium, Bacillus pumilus	It was discovered that EO has antibacterial Properties by inhibiting the formation of biofilm	Cerioli et al., 2018
Syzygium aromaticum Cinnamomum zeylanicum	Streptococcus aureus	The isolated compounds had lower MIC values, indicating a higher antibacterial activity against the <i>Streptococcus aureus</i> and all agent-affected biofilm formation	Budri et al., 2015
Thymus vulgaris Lippia graveolens R. ofcinalis Salvia ofcinalis Ocimum basilicum Zingiber ofcinale	Staphylococcus spp	At the concentration tested, Zofcinal, Rofcinalis, O. basilicum, S. ofcinalis did not demonstrate antibacterial activity, but Tvulgaris and Lgarveolens were equally active but at lower concentrations.	Pozzo et al., 2011
Cinnamon and Trans- cinnamaldehyde	Staphylococcus spp	As a result, EO obtained from cinnamon bark was composed mostly of The EO cinnamaldehyde (68.95%) and eugenol (2.77%), which showed antibacterial activity against <i>Staphylococcus aureus</i> (MIC = 2,000 mg/L). EO from cinnamon leaf was composed of eugenol (73.27) which showed antibacterial activity against <i>Staphylococcus aureus</i>	Budri et al., 2015

#### Ocimum sanctum

The plant *Ocimum sanctum*, also known as Tulsi or basil, belongs to the Lamiaceae family (Anusmitha et al., 2022). A variety of antimicrobial compounds confer therapeutic properties on this herb, including the treatment of diabetes, bronchitis, arthritis, and skin diseases (Goyal et al., 2011). An extract of *Ocimum sanctum* is indicated for the treatment of bovine mastitis (Shafi et al., 2016). It improves phagocytes and phagocyte index, which leads to a decrease in bacterial count (Sharun et al., 2022). In a study, 600 mg/kg body weight of *Ocimum sanctum* leaf powder administered to cows with mastitis twice daily for seven days eliminated 69% of infections and reduced somatic cell counts (Sharun et al., 2022).

#### Cinnamon

The Cinnamon plant is widespread in India, China, and Indonesia, and there are two main types of Cinnamon: Ceylon and Cassia (Hamidpour et al., 2015). There are many health benefits associated with Cinnamon due to its distinctive constituents such as Cinnamyl Alcohol, Cinnamaldehyde, Cinnamic acid, and Coumarin. Some of these activities include antiallergic, antimicrobial, and antioxidant properties (Mohammed, Cinnamon oil in combination with transcinnamaldehyde has been shown to be effective in preventing bacteria biofilm formation and killing the bacteria in the biofilm of the clinical strain S. aureus (Table 2) (Budri et al., 2015). Moreover, Cinnamon Cassia oil has been found to inhibit most pathogens that cause bovine mastitis by disrupting membrane integrity and blocking ATP production (Zhu et al., 2016).

#### Terminalia chebula

The medicinal plant *Terminalia chebula* is widespread in Iran, India, Burma, and Sri Lanka. It is known as black myrobalan, ink tree, or chebulin. It is used extensively in the preparation of many Ayurvedic formulations for infectious diseases such as chronic ulcers and leukorrhea, as well as skin diseases (Pannu et al., 2021). *Terminalia chebula* is useful in the treatment of subclinical bovine mastitis. *Terminalia chebula* extract at a

concentration of 500 g/mL was equally effective as amoxicillin (100 g/mL) against some bacterial such as *E. coli*, *S. aureus*, *Bacillus megaterium*, and *Pseudomonas aeruginosa* (Kher et al., 2019).

#### Prosopis juliflora

Prosopis juliflora (P. juliflora) is an invasive plant species that has been used as firewood in many countries for 150 years (Madhu et al., 2020). Alkaloids extracted from P. juliflora such as julfloridine, juliflorine, julifloricine, juliprosinene can be used as an alternative treatment in the therapy of subclinical bovine mastitis (Shah et al., 2018). Previous studies showed that the combination of Juliflorinine and juliprosinene compound in P. juliflora has an antibacterial effect against E. aureus, Klebsiella pneumoniae, and Pseudomonas aeruginosa (Shah et al., 2018). An intramammary infusion of an affected quarter with normally occurring alkaloids at a concentration of as little as 1%, administered for five consecutive days and nights, resulted in a significant increase in somatic cell count, improved antibacterial activity, and immune modulation simply by amplifying the gene sequence of IL-1 and IL-6 (Shah et al., 2018).

# Limitations of using plant extracts and essential oil

The biological activity of plant extracts and EOs is influenced by various factors, such as the type of solvent, the method of plant extraction, phenotype, storage conditions, water, climate, and soil. These factors cause changes in secondary metabolites responsible for their therapeutic and biological properties (Andrade et al., 2017). Also, using a plant extract, or EO as medicine requires multiple clinical trials to prove its effectiveness. Therefore, future studies should pay more attention to the extraction methods, the formulation of plant extracts and essential oils, and the best methods of using these products (Isman, 2017). Other aspects that should be considered are the effect of extracts and essential oils on the immune system and the composition of milk (Abboud et al., 2015). Therefore, due to the lack of clinical testing, it is suggested that more attention be paid to the clinical evaluation of these extracts and EOs as medicinal products in the future.

#### Conclusion

Alternative therapies for the treatment of mastitis were discussed in detail in this review. Plant extracts and EOs have properties that could be used to treat mastitis. Several experiments examining the therapeutic effects of common local plants and EOs on mastitis were discussed in this review article. Medicinal plants and EOs, due to their naturalness and great diversity, have the potential to be used as alternative medicines. They are attractive to pharmaceutical companies and have shown good profitability. Due to the resistance of microorganisms to current drugs, plant extracts and EOs are considered viable alternatives for treatment of mastitis, which should be proven in future experiments.

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Not applicable

#### **Conflict of interest statements**

The authors declare that there is no conflict of interests.

#### **Ethical approval**

Not applicable.

#### References

- Abboud M., E-l Rammouz R., Jammal B. & Sleiman M. In vitro and in vivo antimicrobial activity of two essential oils Thymus vulgaris and Lavandula angustifolia against bovine *Staphylococcus* and *Streptococcus* mastitis pathogen. *Middle East Journal of Agriculture Research*, 2015, 4, 975-83.
- Alba D.F., da Rosa G., Hanauer D., Saldanha T.F., Souza C.F., Baldissera M.D., Dos Santos D.D., Piovezan A.P, Girardini L.K. & Da Silva A.S. Subclinical mastitis in Lacaune sheep. Causative agents, impacts on milk production, milk quality, oxidative profiles and treatment efficacy of ceftiofur. *Microbial*

- *Pathogenesis*, 2019, 137, 103732. doi.org/10.1016/j.micpath.2019.103732
- Algharib S.A., Dawood A. & Xie S. Nanoparticles for treatment of bovine *Staphylococcus aureus* mastitis. *Drug Delivery*, 2020, 27(1), 292-308. doi.org/10.1080/10717544.2020.1724209
- Álvarez-Martínez F.J., Barrajón-Catalán E., Herranz-López M. & Micol V. Antibacterial plant compounds, extracts and essential oils: An updated review on their effects and putative mechanisms of action. *Phytomedicine*, 2021, 90, 15362690, 153626. doi.org/10.1016/j.phymed.2021.153626
- Ameen F., Reda S.A., El-Shatoury S.A., Riad E.M., Enany M.E., & Alarfaj A.A. Prevalence of antibiotic resistant mastitis pathogens in dairy cows in Egypt and potential biological control agents produced from plant endophytic actinobacteria. *Saudi Journal of Biological Sciences*, 2019, 26(7), 1492-8. doi.org/10.1016/j.sjbs.2019.09.008
- Andi S.A., Nazeri V., Zamani Z. & Hadian J. Morphological diversity of wild Origanum vulgare (Lamiaceae) in Iran. *The Iranian Journal of Botany*, 2011, 17(1), 88-97.
- Andrade K.S., Poncelet D. & Ferreira S.R. Sustainable extraction and encapsulation of pink pepper oil. *Journal of Food Engineering*, 2017, 204, 38-45. doi.org/10.1016/j.jfoodeng.2017.02.020
- Anusmitha K.M., Aruna M., Job J.T., Narayanankutty A., Benil P.B., Rajagopal R., Alfarhan A., & Barcelo D. Phytochemical analysis, antioxidant, anti-inflammatory, antigenotoxic, and anticancer activities of different Ocimum plant extracts prepared by ultrasound-assisted method. *Physiological and Molecular Plant Pathology*, 2022, 117,101746.
  - doi.org/10.1016/j.pmpp.2021.101746
- Atef N.M., Shanab S.M., Negm S.I., & Abbas Y.A. Evaluation of antimicrobial activity of some plant extracts against antibiotic susceptible and resistant bacterial strains causing wound infection. *Bulletin of the National Research Centre*, 2019, 43(1), 1-1. doi.org/10.1186/s42269-019-0184-9
- Baquero F. The 2010 Garrod Lecture: the dimensions of evolution in antibiotic resistance: ex unibus plurum et ex pluribus unum. *Journal of Antimicrobial Chemotherapy*, 2011, 66(8), 1659-72. doi.org/10.1093/jac/dkr214

- Budri P.E., Silva N.C., Bonsaglia E.C., Júnior A.F., Júnior J.A., Doyama J.T., Gonçalves J.L., Santos M.V., Fitzgerald-Hughes D. & Rall V.L. Effect of essential oils of Syzygium aromaticum and Cinnamomum zeylanicum and their major components on biofilm production in *Staphylococcus* aureus strains isolated from milk of cows with mastitis. *Journal of Dairy Science*, 2015, 98(9), 5899-904. doi.org/10.3168/jds.2015-9442
- Cariddi L.N. The role of essential oil of Minthostachys verticillata (Griseb) Epling (Lamiaceae) and its active metabolites in immediate-type hypersensitivity responses. *Recent progress in medicinal plants essential oils II. Houston*, USA, Studium Press, LLC, 2013, 487-95.
- Cecchini M.E., Paoloni C., Campra N., Picco N., Grosso M.C., Perez M.S., Alustiza F., Cariddi N., & Bellingeri R. Nanoemulsion of Minthostachys verticillata essential oil. Invitro evaluation of its antibacterial activity. *Heliyon*, 2021, 7(1), e05896. doi.org/10.1016/j.heliyon. 2021.e05896
- Cerioli M.F., Moliva M.V., Cariddi L.N, & Reinoso E.B. Effect of the essential oil of minthostachys verticillata (Griseb.) epling and limonene on biofilm production in pathogens causing bovine mastitis. *Frontiers in Veterinary Science*, 2018, 5, 146. doi.org/10.3389/fvets.2018.00146
- Cheng W.N. & Han S.G. Bovine mastitis: risk factors, therapeutic strategies, and alternative treatments-A review. *Asian-Australasian journal of animal sciences*. 2020, 33(11), 1699-713. doi.org/10.5713/ajas.20.0156
- Cho B.W., Cha C.N., Lee S.M., Kim M.J., Park J.Y., Yoo C.Y., Son S.E., Kim S & Lee H.J. Therapeutic effect of oregano essential oil on subclinical bovine mastitis caused by *Staphylococcus aureus* and *Escherichia coli. Korean Journal of Veterinary Research*, 2015, 55(4), 253-57. doi.org/10.14405/kjvr.2015.55.4.253.
- Chouhan S., Sharma K. & Guleria S. Antimicrobial activity of some essential oils—present status and future perspectives. *Medicines*, 2017, 4(3), 58. doi.org/10.3390/medicines4030058
- Dal Pozzo M., Loreto É.S., Santurio D.F., Alves S.H., Rossatto L., de Vargas A.C., Viegas J., & da Costa MM. Antibacterial activity of essential oil of cinnamon and trans-

- cinnamaldehyde against *Staphylococcus* spp, isolated from clinical mastitis of cattle and goats. *Acta Scientiae Veterinariae*, 2012, 40(4), 1-5.
- Dal Pozzo M., Santurio D.F., Rossatto L., Vargas A.C., Alves S.H., Loreto E.S, & Viegas J. Activity of essential oils from spices against *Staphylococcus* spp, isolated from bovine mastitis. *Arquivo Brasileiro De Medicina Veterinária E Zootecni*, 2011, 63, 1229-32. doi.org/10.1590/S0102-09352011000500026
- El-Ashker M., Gwida M., Tomaso H., Monecke S., Ehricht R., El-Gohary F. & Hotzel H. *Staphylococci* in cattle and buffaloes with mastitis in Dakahlia Governorate, Egypt. *Journal of Dairy Science*, 2015, 98(11), 7450-9. doi.org/10.3168/jds.2015-9432
- Emami Bistgani Z., Mamedov N, & Lotfy Ashour M. Genus Thymus in Iran—Ethnobotany, Phytochemical, Molecular, and Pharmacological Features. *In Biodiversity, Conservation and Sustainability in Asia*, 2022, 817-48. doi.org/10.1007/978-3-030-73943-0 45
- Escobar F.M., Cariddi L.N., Sabini M.C., Reinoso E., Sutil S.B., Torres C.V., Zanon S.M. & Sabini L.I. Lack of cytotoxic and genotoxic effects of Minthostachys verticillata essential oil: studies in vitro and in vivo. *Food and Chemical Toxicology*, 2012, 50(9), 3062-7. doi.org/10.1016/j.fct.2012.06.018
- Ezzat Alnakip M., Quintela-Baluja M., Böhme K., Fernández-No I., Caamaño-Antelo S., Calo-Mata P. & Barros-Velázquez J. The immunology of mammary gland of dairy ruminants between healthy and inflammatory conditions. *Journal of Veterinary Medicine*, 2014, 1-31. dx.doi.org/10.1155/2014/659801
- Gomes F. & Henriques M. Control of bovine mastitis: old and recent therapeutic approaches. *Current Microbiology*, 2016, 72(4), 377-82. dx.doi.org/10.1007/s00284-015-0958-8
- Griffioen K., Hop G.E., Holstege M.M., Velthuis A.G, & Lam T.J., 1Health4Food–Dutch Mastitis Diagnostics Consortium. Dutch dairy farmers' need for microbiological mastitis diagnostics. *Journal of Dairy Science*, 2016, 99(7), 5551-61. doi.org/10.3168/jds.2015-10816
- Gulluce M., Karadayi M., Guvenalp Z., Ozbek H., Arasoglu T., & Baris O. Isolation of some active compounds from Origanum vulgare L.

- ssp. vulgare and determination of their genotoxic potentials. *Food Chemistry*, 2012, 130(2), 248-53. doi.org/10.1016/j.foodchem.2011.07.024
- Gupta R.E., Kumar S.A. & Khurana R.A. Essential oils and mastitis in dairy animals: A review. *Haryana Vet*, 2020, 59 (S1), 1-9.
- Hamidpour R., Hamidpour M., Hamidpour S. & Shahlari M. Cinnamon from the selection of traditional applications to its novel effects on the inhibition of angiogenesis in cancer cells and prevention of Alzheimer's disease, and a series of functions such as antioxidant, anticholesterol, antidiabetes, antibacterial, antifungal, nematicidal, acaracidal, and repellent activities. *Journal of traditional and complementary medicine*, 2015, 5(2), 6-70. doi.org/10.1016/j.jtcme.2014.11.008
- Hanif M. A., Nisar S., Khan G.S., Mushtaq Z, & Zubair M. Essential oils. *In Essential oil research*, 2019, 3-17. doi.org/10.1007/978-3-030-16546-8 1
- Hosseinzadeh S., Jafarikukhdan A., Hosseini A., & Armand R. The application of medicinal plants in traditional and modern medicine: a review of Thymus vulgaris. *International Journal of Clinical Medicine*, 2015, 6(09), 635. doi.org/10.4236/ijcm.2015.69084
- Ismail Z.B. Molecular characteristics, antibiogram and prevalence of multi-drug resistant *Staphylococcus aureus* (MDRSA) isolated from milk obtained from culled dairy cows and from cows with acute clinical mastitis. *Asian Pacific Journal of Tropical Biomedicine*, 2017, 7(8), 694-7. doi.org/10.1016/j.apjtb.2017.07.005
- Isman M.B. Moving botanical insecticides from the laboratory to the farm. *Industrial Crops and Products*, 2017, 110, 10-4. doi.org/10.1016/j.indcrop.2017.07.012
- Jiang K., Ma X., Guo S., Zhang T., Zhao G., Wu H., Wang X., & Deng G. Anti-inflammatory effects of rosmarinic acid in lipopolysaccharide-induced mastitis in mice. *Inflammation*, 2018, 41(2), 437-48. doi.org/10.1007/s10753-017-0700-8
- Kher M.N., Sheth N.R., & Bhatt V.D. In vitro antibacterial evaluation of Terminalia chebula as an alternative of antibiotics against bovine subclinical mastitis. *Animal Biotechnology*, 2019, 30(2), 151-8. doi.org/10.1080/10495398.2018.1451752

- Kovačević Z., Radinović M., Čabarkapa I., Kladar N, & Božin B. Natural agents against bovine mastitis pathogens. *Optimization of Veterinary Antimicrobial Treatment in Companion and Food Animals*, 2021, 10(2), 205. doi.org/10.3390/antibiotics10020205
- Krömker V., & Leimbach S. Mastitis treatment— Reduction in antibiotic usage in dairy cows. *Reproduction in Domestic Animals*, 2017, 52, 21-9. doi.org/10.1111/rda.13032
- Ksouri S., Djebir S., Bentorki A.A., Gouri A., Hadef Y., & Benakhla A. Antifungal activity of essential oils extract from Origanum floribundum Munby, Rosmarinus officinalis L. and Thymus ciliatus Desf. against Candida albicans isolated from bovine clinical mastitis. *Journal De Mycologie Médicale*, 2017, 27(2), 245-9.
  - doi.org/10.1016/j.mycmed.2017.03.004
- Latifian E. & Arslanoğlu Ş.F. Traditional medicinal plants of Azerbaijan province of Iran. *Agricultural Sciences*, 2018, 9(01), 157. doi.org/10.4236/as.2018.91012
- Lavon Y., Leitner G., Kressel Y., Ezra E., & Wolfenson D. Comparing effects of bovine *Streptococcus* and *Escherichia coli* mastitis on impaired reproductive performance. *Journal of Dairy Science*, 2019, 102 (11), 10587-98. doi.org/10.3168/jds.2019-16673
- Lopes T.S., Fontoura P.S., Oliveira A., Rizzo F.A., Silveira S., & Streck A.F. Use of plant extracts and essential oils in the control of bovine mastitis. *Research in Veterinary Science*, 2020, 131, 186-93. doi.org/10.1016/j.rvsc.2020.04.025
- Madhu P., Mavinkere Rangappa S., Khan A., Al Otaibi A., Al-Zahrani S.A., Pradeep S., Gupta M.K., Boonyasopon P., & Siengchin S. Experimental investigation on the mechanical and morphological behavior of Prosopis juliflora bark fibers/E-glass/carbon fabrics reinforced hybrid polymeric composites for structural applications. *Polymer Composites*, 2020, 41(12), 4983-93. doi.org/10.1002/pc.25768
- Maity S., & Ambatipudi K. Mammary microbial dysbiosis leads to the zoonosis of bovine mastitis: a One-Health perspective. *FEMS microbiology ecology*, 2021, 97(1), 241. doi.org/10.1093/femsec/fiaa241
- Manion C.R., & Widder R.M. Essentials of essential oils. *American Journal of Health-*

- *System Pharmacy*, 2017, 74(9), e153-62. doi.org/10.2146/ajhp151043
- Marinelli L., Di Stefano A., & Cacciatore I. Carvacrol and its derivatives as antibacterial agents. *Phytochemistry reviews*, 2018, 17 (4), 903-21. doi.org/10.1007/s11101-018-9569-x
- Milyuhina A.K., Kyzdarbek U., Romazyaeva I.R. Assessment of antimicrobial activity of medicinal plants' extracts. *InAIP Conference Proceedings*, 2022, 2390 (1), 030059.
- Mohammed M.T. Effects of Cinnamon and Their Beneficial Content on Treatment of Oxidative Stress. *Systematic Reviews in Pharmacy*, 2020, 11(9), 847-50.
- Montironi I. D., Campra N. A., Arsaute S., Cecchini M. E., Raviolo J. M., Braber N. V., Barrios B., Montenegro M., Correa S., Grosso M. C., & Mañas F. Minthostachys verticillata Griseb (Epling.)(Lamiaceae) essential oil orally administered modulates gastrointestinal immunological and oxidative parameters in mice. *Journal of Ethnopharmacology*, 2022, 290, 115078. doi.org/10.1016/j.jep.2022.115078
- Montironi I.D., Reinoso E.B., Paullier V.C., Siri M.I., Pianzzola M.J., Moliva M., Campra N., Bagnis G., LaRocque- de-Freitas I.F., Decote-Ricardo D., & Freire-de-Lima Minthostachys verticillata essential activates macrophage phagocytosis modulates the innate immune response in a murine model of Enterococcus mastitis. Research in Veterinary Science, 2019. 333-44. 125. doi.org/10.1016/j.rvsc.2019.07.015
- Montironi I.D., Cariddi L.N., & Reinoso E.B. Evaluation of the antimicrobial efficacy of Minthostachys verticillata essential oil and limonene against Streptococcus uberis strains isolated from bovine mastitis. *Revista Argentina De Dicrobiologia*, 2016, 48(3), 210-6. doi.org/10.1016/j.ram.2016.04.005
- Mullen, K.A.E. Research from the United States on alternative treatments for mastitis in dairy cattle. *Efficacy of Phyto-Mast*. 2020
- Murinda S.E., Ibekwe A.M., Rodriguez N.G., Quiroz K.L., Mujica A.P. & Osmon K. Shiga Toxin–producing *Escherichia coli* in mastitis: An international perspective. *Foodborne Pathogens and Disease*. 2019, 16(4), 229-43. doi.org/10.1089/fpd.2018.2491
- Ocana-Fuentes A., Arranz-Gutierrez E., Senorans F.J., & Reglero G. Supercritical fluid

- extraction of oregano (Origanum vulgare) essentials oils: Anti-inflammatory properties based on cytokine response on THP-1 macrophages. *Food and Chemical Toxicology*, 2010, 48(6), 1568-75. doi.org/10.1016/j.fct.2010.03.026
- Pankaj G., & Purshotam K. In vitro evaluation of antibacterial activity of various crude leaf extracts of Indian sacred plant, Ocimum sanctum L. *British Microbiology Research Journal*, 2011, 1(3), 70-8.
- Pannu A., Parveen A., Goswami S., & Terminalia chebula: A Review. *Innovat International Journal of Medical & Pharmaceutical Sciences*, 2021, 1-6.
- Paz J.E., Contreras C.R., Munguía A.R., Aguilar C.N., & Inungaray M.L. Phenolic content and antibacterial activity of extracts of Hamelia patens obtained by different extraction methods. *Brazilian Journal of Microbiology*, 2018, 49, 656-61. doi.org/10.1016/j.bjm.2017.03.018.
- Peton V., & Le Loir Y. *Staphylococcus aureus* in veterinary medicine. Infection, *Genetics and Evolution*, 2014, 21, 602-15. doi.org/10.1016/j.meegid.2013.08.011
- Pezzani R., Vitalini S., & Iriti M. Bioactivities of Origanum vulgare L.: An update. *Phytochemistry Reviews*, 2017, 16(6), 1253-68. doi.org/10.1007/s11101-017-9535-z
- Reverter M., Bontemps N., Lecchini D., Banaigs B, & Sasal P. Use of plant extracts in fish aquaculture as an alternative to chemotherapy: current status and future perspectives. *Aquaculture*, 2014, 433, 50-61. doi.org/10.1016/j.aquaculture.2014.05.048
- Reygaert W.C. An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiology*, 2018, 4(3), 482. doi.org/10.3934/microbiol.2018.3.482
- Ribeiro-Santos R., Carvalho-Costa D., Cavaleiro C., Costa H.S., Albuquerque T.G., Castilho M.C., Ramos F., Melo N.R. & Sanches-Silva A. A novel insight on an ancient aromatic plant: The rosemary (Rosmarinus officinalis L.). *Trends in Food Science & Technology*, 2015, 45(2), 355-68. doi.org/10.1016/j.tifs.2015.07.015
- Sadek K., Saleh E., & Ayoub M. Selective, reliable blood and milk bio-markers for diagnosing clinical and subclinical bovine mastitis. *Tropical Animal Health and*

- *Production*, 2017, 49(2), 431-7. doi.org/10.1007/s11250-016-1190-7
- Sarikurkcu C., Zengin G., Oskay M., Uysal S., Ceylan R. & Aktumsek A. Composition, antioxidant, antimicrobial and enzyme inhibition activities of two Origanum vulgare subspecies (subsp. vulgare and subsp. hirtum) essential oils. *Industrial Crops and Products*, 2015, 70, 178-84. doi.org/10.1016/j.indcrop.2015.03.030
- Shafi T.A., Bansal B.K., Gupta D.K., & Nayyar S. Evaluation of immunotherapeutic potential of Ocimum sanctumin bovine subclinical mastitis. *Turkish Journal of Veterinary & Animal Sciences*, 2016, 40(3), 352-8. doi.org/10.3906/vet-1506-96
- Shah K.N., Valand P., Nauriyal D.S. & Joshi C.G. Immunomodulation of IL-1, IL-6 and IL-8 cytokines by Prosopis juliflora alkaloids during bovine sub-clinical mastitis. *3 Biotech*, 2018, 8(10):1-0. doi.org/10.1007/s13205-018-1438-1
- Shakya A.K., Medicinal plants: Future source of new drugs. *International Journal of Herbal Medicine*, 2016, 4(4), 59-64.
- Sharun K., Haritha C.V., Singhal T., Nair S.S., Yatoo M.I., Chakraborty S., Jambagi K., Tuli H.S. & Dhama K. Potential Herbs for Bovine Mastitis Research- A Mini Review. 2022
- Simirgiotis M.J., Burton D., Parra F., López J., Muñoz P., Escobar H. & Parra C. Antioxidant and antibacterial capacities of Origanum vulgare L. essential oil from the arid Andean

- Region of Chile and its chemical characterization by GC-MS. *Metabolites*, 2020, 10(10), 414. doi.org/10.3390/metabo10100414
- Szweda P., Zalewska M., Pilch J., Kot B., & Milewski S. Essential oils as potential antistaphylococcal agents. *Acta Veterinaria-Beograd*, 2018, 68, 95-107. doi.org/10.2478/acve-2018-0008
- Tagousop C.N., Tamokou J.D., Ekom S.E., Ngnokam D. & Voutguenne-Nazabadioko L. Antimicrobial activities of flavonoid glycosides from Graptophyllum grandulosum and their mechanism of antibacterial action. BMC**Complementary** and Alternative Medicine. 18(1), 2018. 1-10. doi.org//10.1186/s12906-018-2321-7
- Thormar H. Lipids and essential oils as antimicrobial agents. 2010 (9780470976678). doi.org/10.1002/9780470976623
- Varela M.F., Stephen J., Lekshmi M., Ojha M., Wenzel N., Sanford L.M., Hernandez A.J., Parvathi A. & Kumar S.H. Bacterial resistance to antimicrobial agents. *Antibiotics*, 2021, 10, (5), 593. doi.org/10.3390/antibiotics10050593
- Zhu H., Du M., Fox L. & Zhu M.J. Bactericidal effects of Cinnamon cassia oil against bovine mastitis bacterial pathogens. *Food Control*, 2016, 66, 291-9. doi.org/10.1016/j.foodcont.2016.02.013