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REVIEW ARTICLE

Prevention and Treatment Effects of Herbal Medicine on Bovine Mastitis

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ABSTRACT

Mastitis, also known as the inflammation of mammary glands, is a major health threat for bovines leading to severe health and economic losses. A significant drop in the production and quality of milk is the characteristic feature of mastitis. There are more than 135 bacterial species known to contribute to the development of mastitis. Among all bacterial species *Staphylococcus aureus, coagulase-negative staphylococci, Escherichia coli, Streptococcus uberis, Streptococcus dysgalactiae,* and *Streptococcus agalactiae* are most reported to cause mastitis. Antimicrobial resistance is a global threat now-a-days because multiple bacterial species have developed resistance against various classes of antimicrobial drugs. Because of the rising issue of antimicrobial resistance, scientists have focused on alternative treatment strategies to overcome this issue. Botanical compounds are well known for their diverse medicinal and biological activities. These properties make them perfect candidates for the treatment of mastitis and the development of new drugs to overcome resistance problem. Flavonoids, saponins, phenolics, and quinones have reported effective mechanisms against mastitis. In this review, we will briefly discuss the pathogenesis of mastitis and different mechanisms of various botanical compounds in order to formulate new potential alternative drugs.

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INTRODUCTION

Mastitis (inflammation of the mammary glands) is the major health problem for cattle as well as buffalos all over the world (Zigo *et al.*, 2021). Mastitis causes a significant drop in milk production of the lactating animals, contributing to a huge economic loss (Ranjan *et al.*, 2022). According to the field surveys of Pakistan, mastitis is ranked number one disease of the dairy animals (Salman *et al.*, 2023). Besides dropping in the milk production of the animal, mastitis also spoils the quality of milk (Long *et al.*, 2023). Mastitis causes significant changes in the chemical composition of milk and alters the cell permeability (Wrońska *et al.*, 2022). Milk from the infected animal cannot be used for further processing and sale purposes (Leone *et al.*, 2022). Bacterial pathogens are the chief culprits of mastitis, but some other factors (injuries of mammary glands and physical trauma) also contribute to the development of the disease (Luo *et al.*, 2022). However, the ratio of mastitis caused by bacterial pathogens and non-infectious causes is 70:30 (Fredebeul-Krein *et al.*, 2022). There are more than 135 types of bacteria that are reported to be involved in the development of mastitis (Tong *et al.*, 2025). Among all bacteria, *Staphylococcus aureus, coagulase-negative staphylococci, Escherichia coli, Streptococcus uberis, Streptococcus dysgalactiae,* and *Streptococcus agalactiae* are most commonly present (Zigo *et al.*, 2022). Mastitis is classified as subclinical and clinical mastitis. It is reported that subclinical mastitis is present in all dairy herds with a prevalence of 5-75% infected cows and 2-40% infected quarters (Khasapane *et al.*, 2023). Subclinical mastitis is determined by measuring the somatic cell count (SCC) in the suspected animals compared with the international threshold amount of SCC (200,000 cells/mL) (Peckler and Adcock, 2025). SCC ≥200,000 cells/mL in the milk sample indicates the likelihood of the presence of subclinical mastitis (Zhang *et al.*, 2022). There are multiple tests used to determine the presence of subclinical mastitis, but the California Mastitis Test is mostly used in the laboratories and field (Tommasoni *et al.*, 2023). There are no apparent clinical signs, or any local inflammation of the mammary gland is present in case of subclinical mastitis, although abnormal milk may appear sometimes, and decline of milk production is present (Bochniarz *et al.*, 2023). In case of clinical mastitis, abnormal milk (fibrin clots and altered color) is present as an inflammatory response to the infection (Velidedeoglu *et al.*, 2021). However, with the increase in inflammation, changes in mammary glands start to occur including redness, heat, pain, and swelling (Mohsin *et al.*, 2022). In severe clinical mastitis cases, systemic inflammation starts to occur that includes anorexia, fever, and shock (Qureshi *et al.*, 2023). Typically, only 1 quarter is infected in the case of clinical mastitis, while multiple quarters can be infected simultaneously in subclinical cases (Alanis *et al.*, 2022). To prevent all the economic losses due to mastitis, we must adopt preventive strategies (Puerto *et al.*, 2021). But to prevent the infection, we must understand the pathogenesis of the disease. Because of the large number of bacteria involved in the development of mastitis, prevention and treatment of the disease is challenging (Goulart and Mellata, 2022). Despite this challenging problem, antimicrobial resistance is one of the major issues that need to be resolved (Coque *et al.*, 2023). Multiple cases of drug resistance are reported against the pathogenic bacteria of mastitis (Awandkar *et al.*, 2022; Cao *et al.*, 2023).

Drug resistance is known as the ability of a microorganism/pathogen to resist the effects of the given drug (Parry *et al.*, 2023). Drug resistance is acknowledged as the chief life-threatening problem of the modern era (Saeed *et al.*, 2023). Microorganisms are developing resistance through multiple mechanisms against different chemical drugs (Murugaiyan *et al.*, 2022). Antimicrobial resistance also develops because of the over and misuse of the drugs (Muteeb *et al.*, 2023). Drug resistance in the case of mastitis can cause more economic loss and results in failure of cure (Ajose *et al.*, 2022; Rashid *et al.*, 2024). Because of the rising problem of resistance, scientists have now focused on the development of new drugs (Coque *et al.*, 2023). The alternative strategies include probiotics, prebiotics, immunogens, peptides, vitamins, and botanical compounds. Among all alternatives, scientists are focused on the use of botanical compounds because of their diverse health and biological properties (Özcan *et al.*, 2021; Hassan *et al.*, 2023; Adeli *et al.*, 2024; Li *et al.*, 2024). These properties include antioxidant, anti-inflammatory, anticancer, antiseptic, antimicrobial, improving immunity and multiple other medicinal properties that make them perfectly suitable for the development of new drugs (Shaikh *et al.*, 2014; Mucha *et al.*, 2021; Cuevas-Cianca *et al.*, 2023; Hegazy *et al.*, 2023; Kalu *et al.*, 2024; Nametov *et al.*, 2024). Most importantly, botanical compounds are easily available and very cost effective (Durazzo *et al.*, 2018). The whole plant was used for prevention and cure of multiple diseases in the past (Ahmed *et al.*, 2021). But in recent years, scientists have focused on specific compounds that are effective in controlling diseases (Rahman *et al.*, 2021). Multiple plant-based compounds have been tested and proven effective in controlling various bacterial, viral, parasitic, and fungal diseases (Fayaz etal., 2019; Rehman et al., 2021; Hussain et al., 2022; Abbas *et al.*, 2025).

To develop new drugs using botanical compounds against mastitis requires complete knowledge of the pathogenesis of mastitis and mechanism of actions of botanical compounds (Ajose *et al.*, 2022; Ucella-Filho *et al.*, 2024). In this review, we will briefly discuss the mechanism of action of different botanical compounds and pathogenesis of the mastitis.

MATERIALS AND METHODS

In this review, we used Google Scholar (www.scolar.google.com) as primary search engine to extract data. Furthermore, other search engines including PubMed (https://pubmed.ncbi.nlm.nih.gov/), Research Gate (www.researchgate.com), and ScienceDirect (http://www.sciencedirect.com/) were used as secondary search engines. To extract data from these search engines we used keywords “Mastitis”, “Animal Mastitis”, “pathogenesis of mastitis in bovines”, “Botanical compounds used against mastitis”, “Polyphenols”, “Flavonoids”, “Saponins”, and “phenolics”. This review only provides qualitative data with no statistical analysis. The quantification of data is beyond the scope of this review.

Pathogenesis of Mastitis: Mastitis is characterized by the inflammation of mammary glands and severely affects milk production and quality (Oviedo-Boyso *et al.*, 2007). About 70% of mastitis cases are developed by multiple pathogenic bacteria, while 30% of the cases are caused by some environmental factors, including physical injury and trauma (Paramasivam *et al.*, 2023). There are more than 135 bacterial species that can cause mastitis, but the most important species include *Staphylococcus aureus, coagulase-negative staphylococci, Escherichia coli, Streptococcus uberis, Streptococcus dysgalactiae,* and *Streptococcus agalactiae* (Krishnamoorthy *et al.*, 2021). The step key for the development of mastitis is colonization of bacteria in mammary glands of the animal (Campos *et al.*, 2022). Bacterial species have developed multiple pathways to facilitate the attachment to the host cells (Ramírez-Larrota and Eckhard, 2022). Biofilm formation is one of the most characteristic of bacteria that aids them in colonization and development of the disease (Sharma *et al.*, 2023). Biofilm is defined as a thin, robust mucilage layer that can adhere to a solid surface and contains a community of bacteria (Nazari *et al.*, 2022). Biofilm synthesis has proven a very effective strategy for pathogenic bacteria to survive within the host (Idrees *et al.*, 2021). Biofilm provides a suitable environment for bacterial growth and also gives nutritional values to the pathogen (Che *et al.*, 2024). *S. aureus* has adhesive matrix molecules that have the ability to identify the microbial surface components in the host (Nappi and Avtaar Singh, 2023). These molecules include Protein A, ClfA, FnBPs, and ClfB that play a significant role in the development of biofilm in the case of mastitis (Moreno *et al.*, 2025). However, Intracellular adhesion (Ica) proteins IcaA, IcaB, IcaC, and IcaD are very crucial for the formation of polysaccharide intercellular adhesion (a major component for the synthesis of biofilm). The synthesis of biofilm is not yet identified in vivo, but polysaccharide intercellular adhesion of *S. aureus* is identified in immunological detection (Peng *et al.*, 2022). The first step after the formation of biofilm is the production of toxins by pathogenic bacteria (Ma *et al.*, 2022). The toxins cause severe injury to the mammary tissues, which causes an increase in the somatic cell count or leukocytes (Carvalho-Sombra *et al.*, 2021). Increased number of somatic cells causes a decline in milk production and poor quality (Toghdory *et al.*, 2022). There are fibrous proteins of keratin present in the teat canal of the animal that bind with the bacteria and disrupt their cell wall (Zigo *et al.*, 2021). But in mastitis these fibrous proteins are severely damaged, and the teat canal may remain open for 1-2 hours after the milking process (Neculai-Valeanu and Ariton, 2022). This will allow other bacterial species and microorganisms to enter the teat canal and cause problems (Ruiz-Romero and Vargas-Bello-Pérez, 2023). After the onset of the infection, an inflammatory response occurs that depends on both pathogenic and host factors (Egyedy and Ametaj, 2022; Gusev *et al.*, 2022). The host factors include age, parity, immune status, somatic cell count and the stage of the lactation of the animal (Sadeghi *et al.*, 2023).

Neutrophils constitute more than 90% of the total leucocytic count present in the mammary secretions and mammary tissues during the early stage of mastitis (Alhussien *et al.*, 2021). Phagocytes in large numbers move towards the mammary glands because of the chemical response produced by the damaged mammary tissues (Jaswal *et al.*, 2022). Multiple oxygen-independent reactants are exposed to bacteria during phagocytosis, including lysozymes, peroxidases, lactoferrin, and hydrolytic enzymes (Rawat *et al.*, 2021). In addition, neutrophils add defensins (antibacterial peptides) in the phagocytic activity (Hao *et al.*, 2021). During this activity of the neutrophils and phagocytosis, the number of somatic cells increase because of the influx of more neutrophils in the lumen of the alveoli (Shangraw and McFadden, 2022). However, the increased number of leukocytes also cause an increment in the somatic cell count (Feng *et al.*, 2021). The mammary ducts are completely blocked because of the clot formation by the aggregation of blood clotting factors and leukocytes (Biswas *et al.*, 2022). The blockage of the mammary ducts results in prevention of complete milk removal and scar formation (Paramasivam *et al.*, 2023). This will ultimately cause permanent damage to the portion of the gland (Xiong *et al.*, 2024). Small pockets are formed because of the clogged milk ducts, making a challenge for the antibiotics to reach (Özhan *et al.*, 2025). Fig. 1 shows the pathogenesis of mastitis by *S. aureus*. Scientists must focus on the specific mechanisms of action of different botanical compounds in order to stop the biofilm synthesis and blockage of the lumen of mammary tissues.

Botanical compounds and their mechanisms of action: Botanical compounds are well known because of their diverse medicinal and biological activities for hundreds of years (Wang *et al.*, 2022b; Elshafie *et al.*, 2023; Gul *et al.*, 2024; Shahzad *et al.*, 2024). The diverse medicinal and biological activities include neuro-protective, anti-oxidative, anti-carcinogenic, anti-mutagenic, anti-inflammatory, cardio-protective, and anti-diabetic properties (Li *et al.*, 2016; Ojukwu *et al.*, 2021; Barbol and Alsayeqh, 2024). Because of these diverse properties of the botanical compounds, they are the best suitable option to be used as alternative control strategies (Li *et al.*, 2018; Deresa and Diriba, 2023; Eltaly *et al.*, 2023; Bagheri *et al.*, 2024). Plant-based products are very cost effective and easily available (Pais *et al.*, 2022). In the past, plants were used to cure and treat various disease but recently scientists have focused on the specific botanical compounds (Chaachouay and Zidane, 2024; Kalu *et al.*, 2024). Multiple botanical compounds have been tested against mastitis and proven effective (Pașca *et al.*, 2020; Kovačević *et al.*, 2022; Ucella-Filho *et al.*, 2024) (Table 1). The major classes of these botanical compounds include

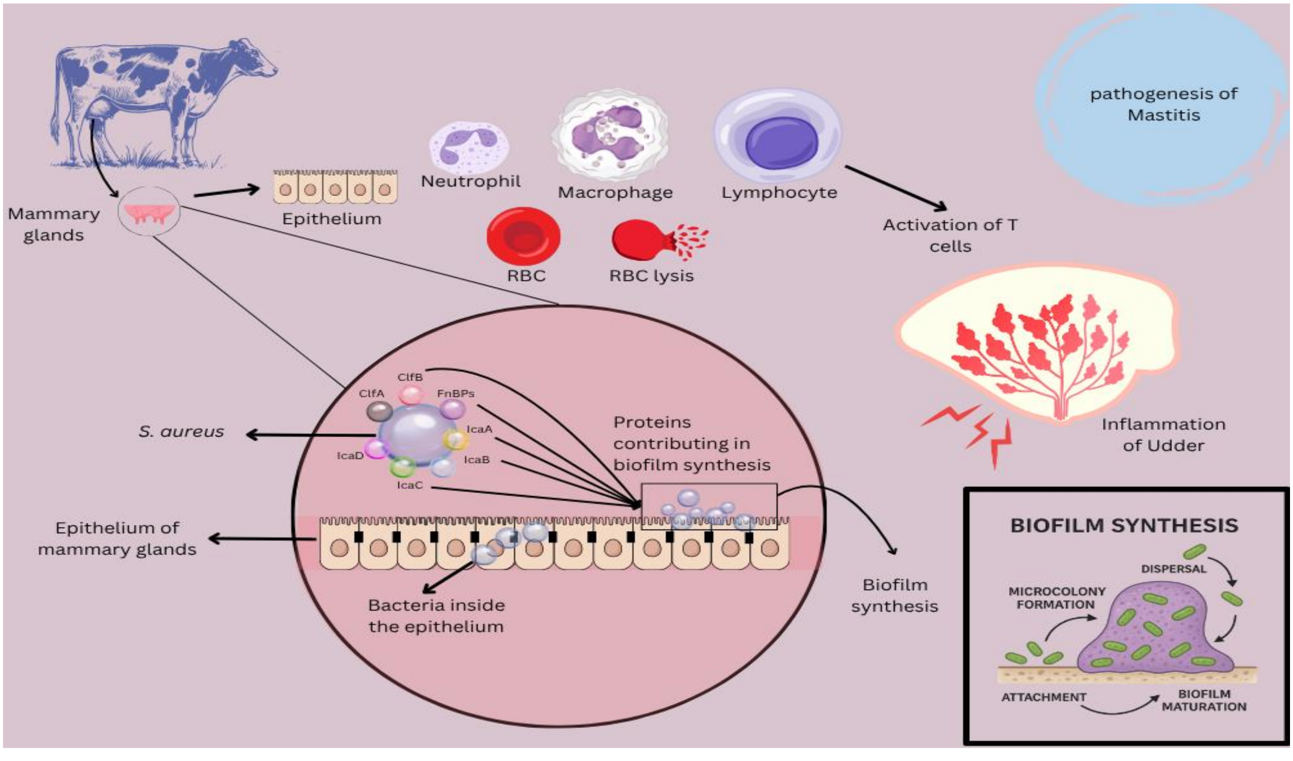

Fig. 1: Role of *S. aureus* in pathogenesis of mastitis.

Table 1: Mechanisms of plant compounds in control of animal mastitis

Plant used	Family of plant used	Compound identified	Class of the compound	Part of the plant used	Type of extract used	Dose rate	Medium of investigation	Animals used for experimentation	Mechanism of action of botanical compounds	Results	references
Allium sativum	Amaryllidaceae	Allicin	organosulfur	N/A	Aqueous	N/A	In vivo	cows	Allicin has great anti-inflammatory activity that results in the arrest of the pathological changes in the udder tissues of lactating animals.	Controlling inflammation of the udder.	(Antanaitis *et al.*, 2023)
Taraxacum mongolicum	Asteraceae	N/A	N/A	Dry whole herb	Aqueous	2.5, 5 and 10g/kg	In vivo	mice	*T. mongolicum* significantly suppressed serum TNF-α and IL-6 production at the doses of 2.5, 5 and 10g/kg.	Inhibits the inflammation of the mammary glands of the lactating mice of age 6-8 weeks.	(Ge *et al.*, 2021)
Lonicera japonica	Caprifoliaceae	Multiple compounds were extracted from *L. japonica*	N/A	Extract was purchased commercially	Ethanolic	1 and 2g/kg DM	In vivo	Holstein dairy cows	*L. japonica* has potential antioxidant and anti-inflammatory mechanisms, but the detailed mechanism against mastitis is scant in this experiment.	1 and 2g LJE/kg DM improved the lactation performance, dry matter intake, enhanced the oxidative and anti-inflammatory capacities during the perinatal period.	(Zhao *et al.*, 2019)
Angelica dahurica	Apiaceae	Furanocoumarin, emodin, polysaccharides, imperatorin, and rhein	Coumarin, quinone, polysaccharides, furanocoumarin, and quinone respectively	Powder of *A. dahurica* was purchased commercially and ethanolic extract was prepared	Ethanolic	N/A	In vivo	Holstein dairy cows	The ethanolic extract reduced the levels of TNF-α, IL-6, and IL-8, in milk. However, the extract showed multiple properties, including detoxification, anti-inflammatory, heat-clearing, and antibacterial activities that aids in the maintenance of the normal histopathology and physiology of the mammary glands of the cows.	Maintained normal histopathology of the udder tissues.	(Yang *et al.*, 2019)
Rheum officinale	Apiaceae	Furanocoumarin, emodin, polysaccharides, imperatorin, and rhein	Coumarin, quinone, polysaccharides, furanocoumarin, and quinone respectively	Powder of *R. officinale* was purchased commercially, and an ethanolic extract was prepared	Ethanolic	N/A	In vivo	Holstein dairy cows	The ethanolic extract reduced the levels of TNF-α, IL-6, and IL-8, in milk. However, the extract showed multiple properties, including detoxification, anti-inflammatory, heat-clearing, and antibacterial activities that aids in the maintenance of the normal histopathology and physiology of the mammary glands of the cows.	Maintained normal histopathology of the udder tissues and inhibits the growth of *S. Aureus.*	(Yang *et al.*, 2019)
Coptis chinensis	Ranunculaceae	N/A	N/A	N/A	Aqueous	N/A	In vitro	N/A	The water extract of *C. chinensis* inhibits multiple microorganisms, including *E. coli, S. aureus,* and *K. Pneumoniae* that are the main culprits of mastitis.	Inhibits the growth of *E. coli, S. aureus,* and *K. Pneumoniae.*	(Jiang *et al.*, 2024)
Camellia sinensis	Theaceae	Tea saponin	saponin	Tea seeds	N/A	2 mg/mL	In vitro	N/A	Extracts from the seeds of *C. sinensis* exhibited potent results in inhibition of the biofilm of *S. aureus* as biofilm plays a vital role in the pathogenesis of the disease, protection of the micro-organism, and development of the resistance.	Arrests the growth and proliferation of a biofilm of *S. aureus*	(Shang *et al.*, 2020)
Quercus robur	Fagaceae	Ellagic acid, vanillic acid, protocatechuic	All identified compounds are phenolic acids except	Bark was purchased	ethanolic and acetone extract	30, 50, and 70% acetone and	In vitro	N/A	The botanical compounds present in the oak bark possibly alter the structure of the cell wall of the	30% of the ethanolic extract showed the highest	(Šukele *et al.*, 2022)

		acid, catechin, and gallic acid,	catechin, it is a flavonoid			ethanolic extract			bacteria that results in the inhibition of pathogenesis of mastitis.	inhibitory zone against the bacteria.	
Calluna vulgaris L.	Ericaceae	Aucubin, chlorogenic acid, flavonoids, arbutin, and tannin metabolites	Iridoid glycoside, polyphenol, flavonoids, quinone, tannins respectively	aerial parts of heather herb	ethanolic and acetone extract	30, 50, and 70% acetone and ethanolic extract	In vitro	N/A	Polyphenolic compounds damage the structural cell wall of *S. aureus* and results in the arrest of proliferation of *S. aureus* in mammary tissues of the female.	30% of the ethanolic extract was effective against *S. Aureus* while the least inhibitory effect was seen in case of *Serratia* and *Streptococcus* bacteria	(Šukele *et al.*, 2022)
Aloe barbadensis	Asphodelaceae	Anthraquinones	Quinone	Whole plant	Methanolic	*A. barbadensis* extract was used at the concentration of 9,10, and 16mg/mL	In vitro	N/A	Anthraquinones cause disruption in the cell membranes of *S. aureus, E. coli, S. uberis*, and methicillin-resistant *S. aureus.*	Cellular destruction of *S. aureus, E. coli, S. uberis*, and Methicillin-resistant *S. aureus.*	(Forno-Bell *et al.*, 2019)
Castanea sativa	Fagaceae	Hydrolyzable tannins	Tannins	Wood	Aqueous	63, 190, 313, 630, and 940mg/mL	In vitro	N/A	Hydrolysable tannins inhibit the extracellular microbial enzymes and cellular growth of the bacteria by damaging the cell membrane and lipid bilayer membrane of *S. aureus.* Tannins also break the cell wall of the bacteria.	Arrests *E. coli* and *S. agalactiae* at the concentrations of 630 and 940mg/mL.	(Prapaiwong et al., 2021)
Punica granatum L.	Lythraceae	Punicalagin	Tannins	Fruit	Hydroalcoholic	10, 25, and 50mg/mL	In vitro	N/A	*P. granatu* extract causes disruption in the cell membrane of the bacteria and alters its permeability, leading to the cellular death. However, the extract has anti-tumor and tissue regenerative properties that aid in the pathogenesis of multiple bacteria, including *E. coli* and *S. aureus.*	100% growth inhibition of *E. coli* and *S. aureus* was achieved at the concentrations of 25 and 50mg/mL	(Silva *et al.*, 2025)

flavonoids, saponins, phenolics, and quinones. We will briefly describe the properties and mechanisms of action of these classes of botanical compounds.

Flavonoids: Flavonoids are yellow colored naturally occurring botanical compounds that belong to family polyphenols (Tahir *et al.*, 2023; Kuljarusnont *et al.*, 2024). Flavonoids are complex compounds, but their simplest structure contains 2 phenyl rings, which are attached to a heterocyclic ring (Zhang *et al.*, 2023). Flavonoids are mostly present in free and aglycone and glycosidic-bond forms in different parts of the plants (Xie *et al.*, 2022). However, the glycosidic-bond form of flavonoids is most commonly used in diet plans (Liu *et al.*, 2023). Flavonoids are widely used as preventive and medicinal agents in multiple diseases because of their diverse biological activities (Chen *et al.*, 2023).

Multiple studies have reported the effectiveness of various compounds of flavonoids against mastitis (Disbanchong *et al.*, 2021; Burmańczuk *et al.*, 2022; Gutiérrez-Reinoso *et al.*, 2023; Gao *et al.*, 2024; Haj Hasan *et al.*, 2024; Iqbal *et al.*, 2024). There are specific proteins known as multidrug efflux pump (MEP) present in the cell membrane that are responsible for the removal of different antimicrobial drugs from the bacterial cell (Salikin *et al.*, 2024). MEP is responsible for active transport of various toxins and antibiotics out of the bacterial cell, providing the bacteria suitable environment to grow (Gaurav *et al.*, 2023). MEP hinders the effectiveness of antibacterial drugs and reduces their intracellular concentration (Nishino *et al.*, 2021). Furthermore, MEP can also transport virulent factors and signaling molecules of bacteria that aid in the pathogenicity and survival of bacteria in the mammary tissues (Pasqua *et al.*, 2021). These mechanisms lead to the failure of antibiotic treatment (Elshobary *et al.*, 2025). However, flavonoids have great potential to inhibit MEP, which results in the alteration of the cell membrane of bacteria, leading to cellular death (Donadio *et al.*, 2021; Huang *et al.*, 2022). Flavonoids have shown activity against multiple bacteria that are involved in the pathogenesis of mastitis, especially *S. aureus* (Campos *et al.*, 2022; Haj Hasan *et al.*, 2024). Different compounds of flavonoids cause disruption in the membrane permeability of the bacteria, which causes an arrest of the bacterial growth in the mammary gland (Xu *et al.*, 2022). However, some compounds of the flavonoids reported causing the aggregation of bacteria and nutritional deficiency for *S. aureus* (Ahmad-Mansour *et al.*, 2021; Wen *et al.*, 2021; Veiko *et al.*, 2023). The multi-faceted approach of flavonoids makes them perfect candidates for the development of new drugs to control mastitis.

Saponins: Saponins form foamy/soapy appearance when agitated with water (El Aziz *et al.*, 2019). Basic structure of the saponins contain minimum one glycosidic linkage between non-sugar organic molecule (aglycone) and sugar chain (glycone) (Alamgir, 2018; Abduljawad *et al.*, 2022). In the past, saponins were most commonly used to make soap and drug adjuvants because of their soapy nature (Rai *et al.*, 2021). But in recent years, scientists have tested various compounds of saponins against multiple diseases (Man *et al.*, 2010). Saponins found in naturally occurring plants have shown potent activity against multiple pathogenic bacteria (Khan *et al.*, 2018; Tagousop *et al.*, 2018; Dong *et al.*, 2020). Saponins are found to have great potential to increase immunity by stimulating cytokines and chemokines (Sun *et al.*, 2014). They aid in the differentiation and proliferation of T-cells into CD4+ T-helper cells (Ho *et al.*, 2023). After multiple research activities performed on saponins, they are found to be responsible for the immune cell recruitment and managing the intracellular signalling pathway (Den Brok *et al.*, 2016; Chen *et al.*, 2024a). However, saponins have great anti-inflammatory potential that allows them to combat mastitis (Pathak *et al.*, 2024).

Primarily, saponins are reported to destroy the cell membranes of *S. aureus* and *E. coli* (Wei *et al.*, 2025). The destruction mechanism of saponins is successful because of the amphipathic nature (hydrophilic and lipophilic) (Liao *et al.*, 2021). Lipophilic and hydrophilic components of saponin compounds interact and destabilize the cell membranes of *E. coli* and *S. aureus* (Rojewska *et al.*, 2023). This disruption in the cell membrane of pathogenic bacteria causes the leakage of the cellular material, leading to cell death (Wijesundara *et al.*, 2021). However, saponins increase the cell membrane permeability of *S. aureus* and *E. Coli* that allows different antibiotics to enter the cell and perform their job (Grzywaczyk *et al.*, 2023). This synergistic effect of the saponins with antibacterial drugs is proven very effective against the control of mastitis (Srichok *et al.*, 2022). However, further research must be conducted on saponins to check their safety index and toxicity in animals.

Phenolics: Phenolics are a very broad class of botanical compounds having one or more hydroxyl groups attached to benzene (aromatic) ring (Kisiriko *et al.*, 2021). Phenolics are widely distributed in different parts of the plant, including leaves, roots, stems, seeds, and fruits (Nurzyńska-Wierdak, 2023). However, higher concentrations of phenolics are found in stems and leaves (Guo *et al.*, 2021). Phenolics range from very simple molecules to very complex structures having hydroxyl groups directly attached to the benzene ring (Chen *et al.*, 2024b). Phenolics are well known for their diverse biological activities and health activities (Sun and Shahrajabian, 2023). Multiple health properties of phenolics include antidiabetic effects, antioxidants, and effectiveness against cardiovascular and neurodegenerative disorders (Fatima *et al.*, 2023).

Phenolics have potential activity to interact with the DNA of *S. aureus, E. coli* and various other pathogenic bacteria (Morshdy *et al.*, 2023). Phenolics interact with the bacterial DNA and cause damage to its helical structure, leading to the arrest of transcription, protein synthesis, and replication processes (Yilmaz *et al.*, 2022). Damage to the DNA of *S. aureus* and *E. coli* causes instability and directly leads to cellular death (Wang *et al.*, 2022a). However, phenolics have multiple mechanisms of action. Phenolics alter the cell membrane permeability of *S. aureus* and *E. coli,* causing the cell membrane to become more permeable and rupture (Davidova *et al.*, 2024). Damage to the integrity of the cell membrane of bacteria causes the outflow of internal material of the cell, leading to cell death (Jeyanthi *et al.*, 2021). Creating oxidative stress is another mechanism that is involved in killing the bacteria (Ecevit *et al.*, 2022). Phenolics create reactive oxygen species, which generates oxidative stress conditions in the bacterial cell (Sahu *et al.*, 2022). Oxidative stress leads to cellular damage and ultimately death (Behl *et al.*, 2021). Phenolics can be good candidates for the development of new alternative drugs, but their toxicity and safety index must be tested.

Quinones: The name 'Quinone' is derived from quinic acid because they are obtained after the oxidation of quinic acid (Santarcangelo *et al.*, 2024). Quinones are cyclic organic compounds having a conjugated system of carbonyl groups having double bonds (Dulo *et al.*, 2021). The formation of the double bond in their chemical structure results in the formation of cyclic diones (Dong *et al.*, 2024). Quinones attract scientists because of their different medical and health activities. Quinones form a major class of anticancer drugs, which attract pharmacologists as well (Dahlem Junior *et al.*, 2022).

Multiple compounds of the quinones are carriers of electrons that play a significant role in the respiration of *S. aureus* in the electron transport chain (Pires *et al.*, 2024; Sena *et al.*, 2024). TNF-α and IL-6 are pro-inflammatory cytokines, while IL-8 are chemokines which play a significant role in mastitis (Vitenberga-Verza *et al.*, 2022). The pro-inflammatory cytokines activate the immune system, leading to the inflammatory response in mastitis (Khan *et al.*, 2023). While chemokines activate and attract neutrophils, which also results in inflammatory response (Xu *et al.*, 2023). Multiple studies have been reported that various compounds of quinones exhibit anti-inflammatory activity against TNF-α, IL-6, and IL-8 related to mastitis (Li *et al.*, 2021; Song *et al.*, 2022; Gao *et al.*, 2024; Tan *et al.*, 2024). The anti-inflammatory response of quinone restricts the accumulation of immune cells, which results in the reduction of tissue damage and the extent of inflammation (Mucha *et al.*, 2021). However, some compounds of quinones are reported to have the mechanism of alteration of the cell membrane and destruction of cell wall of *S. aureus and E. coli* (Ecevit *et al.*, 2022; Zhao *et al.*, 2022). Any damage to the cell wall or cell membrane leads to cellular instability ultimately cell death. Further research must be conducted to check the toxicity and safety indices of quinones.

Conclusions: Mastitis, also known as the inflammation of mammary glands, is a major health threat for bovines, leading to severe health and economic losses. Mastitis causes a significant drop in the production of milk and alterations in the milk quality (fibrin clots and altered color). There are more than 135 bacterial species known to contribute to the development of mastitis. Among all bacterial species *Staphylococcus aureus, coagulase-negative staphylococci, Escherichia coli, Streptococcus uberis, Streptococcus dysgalactiae,* and *Streptococcus agalactiae* are most reported to be present in mastitis. Antimicrobial resistance is a global threat now-a-days because multiple bacterial species have developed resistance against various classes of antimicrobial drugs. Because of the rising issue of antimicrobial resistance, scientists have focused on alternative treatment strategies to overcome this issue. There are multiple alternative strategies suggested, but botanical compounds have most promising results against mastitis. Botanical compounds are well known for their diverse medicinal and biological activities. Various health properties of botanical compounds include antioxidants, anti-inflammatory, anticancer, antimicrobial, and multiple other medicinal properties. These properties make them perfect candidates for the treatment of mastitis and the development of new drugs to overcome resistance problem. There are different classes of botanical compounds that have proven to have effective mechanisms against mastitis. These botanical compounds include flavonoids, saponins, phenolics, and quinones. Further research must be conducted to check the toxicity of the botanical compounds and their safety index.

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