International Journal of Enhanced Research in Educational Development (IJERED)
ISSN: 2320-8708, Vol. 12 Issue 1, Jan.-Feb., 2024, Impact Factor: 8.376

A Review On: Potential Alternative Treatment for Bovine Mastitis

Disha P. Shilwant[1], Digvijay N. Mokashi[2], Somnath A. Ithape[3], Mr Prashant S, Bhosale[4]

[1]Bachelor of Pharmacy SEF's SarSam College of Pharmacy, Baramati, Maharashtra, India -413102
[2]Bachelor of Pharmacy SEF's SarSam College of Pharmacy, Baramati, Maharashtra, India -413102
[3]Bachelor of Pharmacy SEF's SarSam College of Pharmacy, Baramati, Maharashtra, India -413102
[4]Assistant Professor (M.Pharm), SEF's SarSam College of Pharmacy, Baramati, Maharashtra, India -413102

ABSTRACT

The most prevalent illness affecting dairy cattle is bovine mastitis, which is an infection of the mammary gland that results in lower milk quality and a decreased output, which can lead to financial losses. A wide range of gram-positive and gram-negative bacteria are the etiological agents. They can be environmental (e.g., Escherichia coli, Enterococcus spp., coagulase-negative Staphylococcus, Streptococcus uberis) or contagious (e.g., Staphylococcus aureus, Streptococcus agalactiae, Mycoplasma spp.). While general efforts to avoid new instances of mastitis, such as improved milking hygiene, post-milking teat cleaning, and maintenance of milking machinery, are important, antibiotics are the principal therapy for current mastitis infections. However, the dairy industries reduced their usage of antibiotics due to worries about antibiotic-resistant bacteria emerging from the widespread use of antibiotics. This review provides the information about the potential alternative for the modern and chemical methods to treat mastitis to avoid the risk of chemicals to enter into the healthy body of living beings as well as to prevent the side effects caused due the chemicals used for the treatment of the effected cattle.

Index Terms: Bovine Mastitis, ranching, milk, udder, teats, Staphylococcus, Streptococcus, pathogens.

INTRODUCTION

Bovine Mastitis, a disease that frequently and typically appears in the dairy cattle which is caused due the microbial and various etiological agents where they produce poisonous toxins and gives rise to inflammation and injuries to the udder (mammary gland) of the cattle that results in physical trauma as well as lowers the milk yield and unsympathetically effects the quality of the milk products. [1]

Ranching and their process are a growing factor in the economic sector globally. The source of income and the earning effects of the Ranching economy is high. Over billion of peoples depend upon livestock and is the most important source of income for the poor and mainly for the women in the countries which are developing. Among these over 60% of rural people depend on the livestock for their livelihood. Therefore Ranching finance is essential for the overall capital stock in the world of agriculture. [2]

Considering the growing population, milk consumption has been increasing to an average of 10-15 million tonnes per year approximately over the global. Several Asian and European countries are the large milk consumers, from which China and India are the countries which demand the higher rate of milk and other dairy products for their daily needs. Countries like USA, Europe, United Kingdom, Australia and South Africa faces the largest economic losses due to this severe disease, resulting in long term in low production of milk. [2]

Usually, the overall estimation of total cost failure faced due to Bovine Mastitis is up to $147 (12,239.73 Indian rupees) approximately which leads to reduction of milk production for 70% to 75% of the total loss. According to the survey in India, the net loss of indigenous cows is Rs.1695 per cow reported higher as compared to the cross breed cows which is Rs.1597.64 per cow effected by Bovine Mastitis. [3]

For past 7 decades menacingly researchers are comporting the solution to treat Bovine Mastitis but unfortunately this a challenging situation for both the veterinarians as well as for the pharmacy researchers to particularly find a solution to treatment and control over this disease. A controlled evaluation tactics should be executed to control this lethal disease

of ranching animals to avoid the economic damages of the farmers. To aware the farmers and the researchers, it's important to understand the detailed mechanism of mastitis. For this we have to compile all the detailed information and researched data from all over the world and update our framers and researchers for the prevention of heavy losses faced due to this diseases. [4]

This review focus attention on the agents and circumstances causing mastitis with their diagnosis and the three system treatment medicaments for the udder health in the dairy cattle.

Let's get acquainted by the Mastitis:
Mastitis is a disease affecting dairy cows' udders, which are the mammary organs. The term comes from the Greek words 'Mastos', meaning udder tissues, and 'tits', meaning irritation. The nipple waterway and mammary tissues in milk-delivering animals are affected by microbial and etiological factors. The nipple end plays a crucial role in protecting against microorganisms. A smooth muscle called sphincter covers the external part of the nipple trench, preventing microorganisms from entering and preventing milk delivery.

The internal side of the nipple trench is fixed with keratin cells, which damage this lining and increases the powerlessness of the nipple channel to bacterial attacks. The stringy keratin ties electrostatically to microorganisms, causing mastitis. This leads to the bacterial cell wall reversing and increasing osmotic pressure, leading to the lysis of attacking microorganisms. Keratin structure plays a significant role in supporting microorganisms and deflecting their resettlement into the organ storage.

In pre-pubertal cows, the mammary organ is considered a sterile environment before colostrogenesis, which is the development of colostrum. During the shedding period, microbes near the nipple can enter the nipple trench, causing damage to the keratin or mucous layers. This attack on microorganisms enters the nipple trench and replicates in the udder tissues, leading to diseases.[6]

Classification:
These disease is assorted into three types based on their etiologic causes in the cow and these types are:

1.**Contagious Mastitis:-** It is caused due the pathogen present in teat or the udder of the cattle which may pass on to other cow during the milking or cleaning process and it further divided three sub types:

1.1 ***Clinical mastitis*** is characterized by inflammation, swelling, redness, and pain in cow udder tissues, clotting, discoloration of milk, fever, and loss of appetite. It is subdivided into pre-acute, acute, and sub-acute based on severity. Pre-acute mastitis reduces milk yield and shows systemic signs, while acute mastitis shows milder symptoms and sub-acute mastitis has minimal inflammation without visible systemic signs.[7]

1.2 ***Subclinical mastitis:*** It is described by change in milk creation (SCC, leukocytes and epithelial cells, changes in milk pH and particle fixation) with no clinical indications of gross aggravation or milk irregularities. In solid lactating mammary organ, the milk SCC is frequently <100,000 cells/ml of milk while can increment to >1,000,000 cells/ml of milk during subclinical mastitis. The central point influencing the SCC at the group and individual level is the presence of intra mammary contaminations.[8]

1.3 ***Chronic Mastitis:*** Ongoing mastitis: an incendiary interaction exists for quite a long time, and may go on from lactation of one to the next lactation. It exists as subclinical however show periodical eruptions sub-intense or intense structure that keep going for a brief timeframe.

2. **Environmental Mastitis: -** It is brought about by life forms, for example, Escherichia coli which don't typically live on the skin or in the udder yet which enter the nipple waterway when the cow interacts with a defiled climate. The microorganisms regularly found in excrement bedding materials, and feed.

3**. Summer Mastitis: -** A third kind of mastitis, alluded to as summer mastitis, is an intense sickness of dry cows and yearlings which makes broad and excruciating harm the udder. The tainted quarter is for all time harmed bringing about early separating of the cow. Disease is bound to happen when cows are in climate where the nipples can undoubtedly be presented to harm and high fly populaces. The clinical indications of summer mastitis are blistering, hard and enlarged quarter in relationship with a thick discharge portrayed by a foul smell. [9]

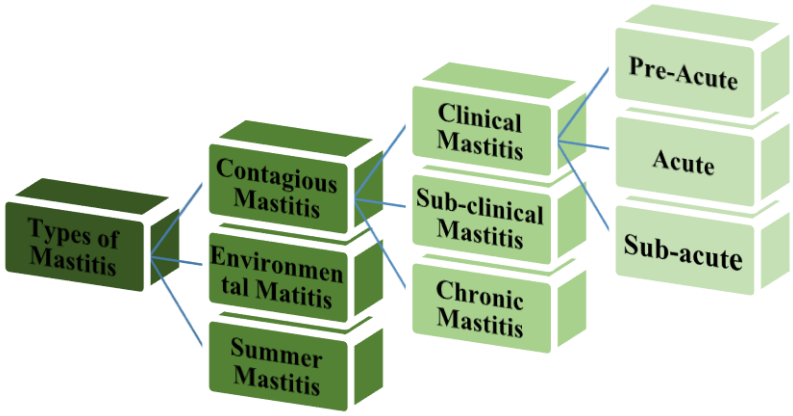

Fig no: Types of Bovine mastitis

What causes Mastitis?

Mastitis, a common dairy disease, is primarily caused by microbiological diseases, with over 150 pathogenic microorganisms identified as the main cause. While microbes, organisms, and yeasts may play a role, microorganisms have a significant impact. Ox-like mastitis is primarily bacterial in origin, often referred to as infectious or natural. Infectious microorganisms like S. aureus, Strep. dysgalactiae, and Strep. agalactiae cause subclinical contaminations, while natural microorganisms like Strep. uberis and Enterobacteriacae like E. coli reproduce quickly after infection and cause a quick safe reaction. The key etiological factors responsible for mastitis contamination in dairy cows can be divided into various groups of organic entities, including infectious microorganisms, ecological microbes, astute microbes, or other less frequently causing organisms.

Contagious Pathogens:

Staphylococcus aureus, Streptococcus agalactiae, and Mycoplasma bovis are common sources of disease in contaminated cows, particularly during milkings. Staphylococcus aureus colonizes the areola skin and enters the mammary organ channel, leading to subclinical mastitis and a deep-rooted disease. It is difficult to eliminate in comparison to Streptococcus agalactiae, as the microorganisms can create chemicals and poisons that cause damage to udder tissue and allow the microbes to enter the tissue.

Streptococcus agalactiae is a committed microbe of the mammary organ that spreads easily among cows during draining, causing discomfort, growth, and subclinical mastitis. Despite the presence of simple clinical signs without abnormal milk production, low production rates and high SCC are generally associated with these infections. Mycoplasma species are more uncommon than Streptococcus agalactiae and Staphylococcus aureus, but they cause organ fibrosis, abscesses, and lymphatic knobs fibrosis.

Mycoplasma species are more common than Streptococcus agalactiae and Staphylococcus aureus, but they can cause organ fibrosis, abscesses, and lymphatic knobs fibrosis. Mycoplasmosis is typically associated with mastitis flare-ups, new animal contact, past respiratory or articular diseases, and resistance to anti-microbial treatment. When repetitivemastitis, non-signs disease, and ineffective treatment are observed, a mycoplasma infection is suspected. [10]

Environmental Mastitis:

Numerous Gram-positive and Gram-negative species are present in cows, which are responsible for most clinical cases. These microbes, such as Streptococcus uberis, Streptococcus equinus, Enterococcus faecalis, and Enterococcus faecium, require dampness, good pH, and natural materials for endurance and enter the organ through the nipple channel. They live in soil, bedding materials, compost, and other natural matter.

Efforts at controlling natural mastitis should focus on the cleanliness of a cow's working environment and tidiness. Mastitis caused by ecological creatures is sharp and can be severe if the host's resistance is compromised or if sterilization and cleanliness are not adequately rehearsed.

Mekonnen and Tesfaye (2010) found that infectious microorganisms like Coagulase negative staphylococci (CNS), S. aureus, S. agalactiae, and S. dysgalactiae, as well as ecological microorganisms like coliforms, were the major etiology of mastitis in smallholder dairy ranches in Adama, Ethiopia. Watts (2002) identified bacterial segregates in milk from dairy groups in and around Gondar, Ethiopia, including Staphylococcus aureus, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptcoccusuberis, Escherichia coli, CNS, Micrococcus species, Bacillus cereus, Corynebacteriumbovis, and Actinomycespyogens. Staphylococcus aureus is the most common type of cow-like mastitis microbe. [11]

Epidemiology:
Mastitis is a disease involving the pathogen, host, and environment. Factors include breed, mammary gland state, and teat canal anatomy. Agents include survival, colonization, and adhesion. Environmental factors include milking practices, housing, and bedding. Body defence mechanisms prevent pathogenic microbes from entering the mammary gland. Genetically controlled antibacterial factors depend on lactation stage and udder health. Management, feeding, hygiene, and virulence contribute to the disease. Stress factors can increase somatic cell count without mastitis.[12]

Mastitis in dairy cows is caused by various pathogens, with three distinct modes: Contagious, Opportunistic/Environmental, and Vector infectious Patterns, each with varying mechanisms and clinical subtypes.

Contagious diseases pattern: contagious diseases, such as S. agalactiae and S. aureus, are the most common mode of disease transmission in dairy cattle. Epidemics like Nocardiaspp, Mycoplasma spp, and environmental streptococci remain endemic when the mean number of susceptible individuals is significantly larger than one. Prevention programs aim to reduce new infections by optimizing milking procedures, reducing shedders, and optimizing cow immune function. Eliminating existing infections reduces exposure of susceptible quarters.[13]

Environmental diseases pattern Mastitis is a disease caused by a complex interplay of microorganisms, host factors, and the environment. The most significant microorganisms are

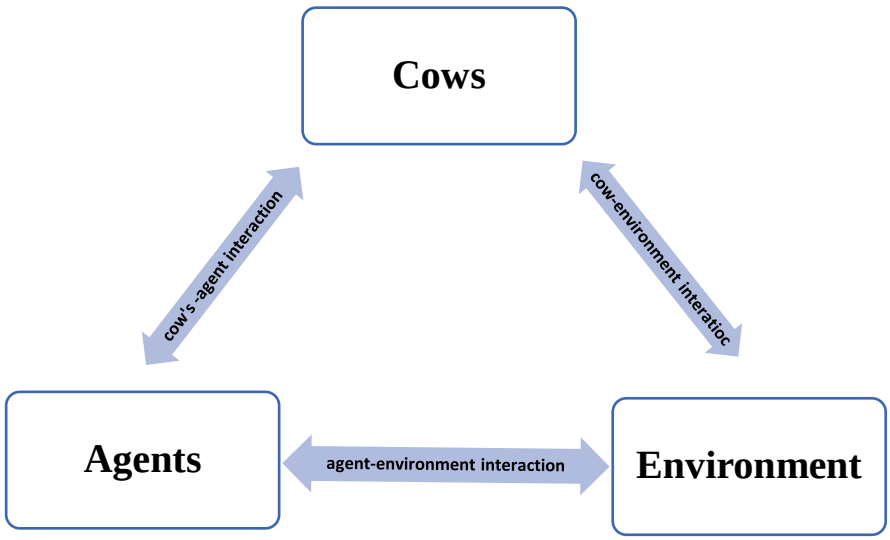

Fig no2: Epidemiologic infection traids

E.coli and Klebsiella spp. and environmental streptococci. Serum resistance and antigen determinants influence clinical severity. However, a solution based solely on microorganism reduction may not be effective. Host factors, such as genetic predisposition, anatomic characteristics, nutritional status, lactation stage, parity, and management procedures, also contribute to resistance. Most infections result in minimal clinical signs.Cows' health can be influenced by various factors, including blood leukocyte count, antibodies, age, metabolic status, mineral nutrition, peri-parturient stress, and milk production level. Early lactation cows are particularly susceptible to clinical mastitis, with a higher risk of severe illness. Environmental factors, such as manure, bedding, feeds, dirt, mud, and water, also affect cow exposure to microorganisms. Studies have linked cleanliness in barns and bedding colony counts with infection incidence. Most infections with coliform and environmental streptococci occur in the last two weeks before calving.[14]

Vector Infection Pattern: Cow health is influenced by factors like blood leukocyte count, antibodies, age, metabolic status, mineral nutrition, peri-parturient stress, and milk production. Early lactation cows are more susceptible to clinical mastitis. Environmental factors like manure, bedding, feeds, dirt, mud, and water also affect cow exposure to microorganisms, with most infections occurring before calving.[15]

Transmission:
Mastitis can be transmitted through two main modes: contagious transmission, which occurs during milking, and environmental transmission, which originates from the environment such as bedding, manure, or water. Contagious transmission occurs when cows with mastitis are the main source of infection, and the bacteria that cause the infection spread through the milker's hands, udder cloths, or the milking machine. To prevent the spread of infection, milking infected cows last or using a separate unit is recommended. Environmental transmission occurs when bedding, manure, or water are contaminated with bacteria, which can accumulate in milking machines. People can also be a direct source of infection for animals, as many mastitis-causing bacteria occur in people as well as cattle. The human-to-animal route of transmission has various names, but none are particularly attractive.[16]

Signs and Symptoms:
The signs and symptoms may vary according to the severity of the infection and the inflammation of the disease in the cattle.

- Thickening and elongation of the teats.
- Irritation (due to flies fly around) causes the cow to kick the udder often.
- Inflammation of udder
- Change in the udder temperature.
- Swelling, redness, and pain.
- Mucus, clots and flakes in milk.
- Changes in the concentrations of main components of milk i.e. lactose and somatic cell count.

Inflammation in cattle leads to reduced locomotion and udder irritation, resulting in foot sprains, limpness, fatigue, weight loss, and high body temperature. This condition causes the animal to appear tired, lose weight, and have a high body temperature.

Diagnosis:
The California Mastitis Test (CMT) is a simple cow-side indicator for subclinical mastitis, using somatic cell count estimation of milk. A score of 2 or 3 is considered positive. It's inexpensive, nontechnical, and can improve dairy animal management and prevent mastitis.

Somatic cell counting:
Somatic cell counting is a method used to measure the number of epithelial and leukocytes secreting through milk. Inflammation, such as mastitis, can increase somatic cell count due to the migration of neutrophils. Factors like infection level, lactation stage, age, breed, parity, season, stress, diurnal variation, and milk transport management can influence the occurrence of mastitis. Bulk Tank Somatic Cell Count (BTSCC) is also used to measure milk quality.[20]

In- vitro culture based diagnosis:
In vitro culture is the gold standard test for mastitis, allowing for the isolation of bacteria, viruses, and fungal pathogens in milk samples. However, it is time-consuming, cumbersome, and requires specific mediums. Fungal pathogens can be easily isolated, but time-consuming. Culture negative results require further study due to their clinical relevance.

PCR based diagnosis:
PCR-based diagnosis in mastitis milk samples is less time-consuming and DNA-based, detecting fewer organisms than culture methods. Tools like.165 and 165-235 spacer rRNA genes are used for identification.[21]

Risk factors
Genetic Aspects: Mastitis in dairy cows is primarily caused by genetic factors, with increased milk yield selection negatively impacting mammary gland health. This disease is prevalent in high-production herds raised in intensive farming conditions, causing significant health issues.

Udder Structure: Udder structure plays a significant role in cow health, with unequally developed quarters and long teats increasing susceptibility to infections. Cows with a pendulous udder or long, funnel-shaped teats are at a higher risk of subclinical mastitis. Mastitis is observed in cows with smaller teats, shorter teat canals, and larger teat base and diameter. The cross-sectional area of the teat canal also affects susceptibility to infection.

Types and breed of cows: Mastitis is a prevalent issue in dairy herds worldwide, affecting every herd. Beef cows have a mammary gland that produces milk for their young, and their udder is naturally empty, preventing mechanical damage or acute infections. As a result, mastitis is less closely monitored in beef cow herds, as the calves typically empty their udder multiple times a day.

Age and stage of lactation in cows: Mastitis in cows is linked to factors such as age and lactation stage. Older cows may have wider teat canals due to frequent milking or partially open ones. The age also affects mammary epithelium permeability, which can be affected by previous inflammatory states. Clinical mastitis risk is up to four times higher in heifers with an infected udder before parturition. Mastitis cases are more common after parturition, early lactation, and during the first 2-3 weeks of the dry period due to increased oxidative stress and lower antioxidant defence mechanisms.

Hygiene and milking system: Maintaining cleanliness while milking is especially crucial for preventing and treating contagious mastitis in the herd, cows housed in herds where hand washing is a regular practice and milking is done in a traditional manner had a reduced chance of developing subclinical mastitis than do cows in herds where hand washing is not practiced.

Dry period of cows: The dry period significantly impacts cows' udder health and increases mastitis risk. It involves physiological, metabolic, and hormonal changes, primarily involving gland tissue regeneration. The optimal dry period is 40-60 days, but shortening reduces udder resistance to inflammatory states.

Body conditions: High-yielding dairy cows often have a negative energy balance after calving, which can affect their immune and metabolic systems. Chronic deficiencies in energy, protein, minerals, or vitamins can increase disease susceptibility. Optimal feeding during early lactation and dry periods may prevent mastitis. Cows with high BCS may experience a longer immunosuppressive period, potentially affecting mastitis risk.

Hygiene score: The environment in which dairy cows are kept significantly impacts their health and welfare. A clean and comfortable shelter is crucial for their longevity and health. Low hygiene can lead to high mastitis risk and worsened lameness. Studies show a relationship between shelter hygiene, clean cows, and low somatic cell count in mixed milk. Global hazards like bedding type, slurry removal, and housing type can also affect environmental mastitis frequency.[17-19]

Modern treatment and their alternative medicaments:
The National Institute for Research in Dairy (NIRD) introduced a five-point plan in the 1960s to control contagious mastitis pathogens. The plan includes identifying and treating clinical cases, post-milking teat disinfection, DCT, culling chronic cases, and routine machine maintenance. However, it is not effective against environmental pathogens and should be combined with other strategies.

Antibiotic Therapy:
Mastitis is a common dairy disease that can be treated with antibiotics like penicillin, ampicillin, tetracycline, and gentamycin. The dry cow period is crucial for controlling and inhibiting the progression of mastitis, and it is essential to monitor cow health before milking. The California mastitis test (CMT) is used to detect chronic mastitis cases. After milking, antibiotics are applied to the cow's udder through canal teat and teat sealant. Long-persistence antibiotics are recommended for better cure rates. However, antibiotic residues in milk can pose a concern, and in severe cases, parenteral administration is recommended. Long-acting antibiotics are not suitable for mastitis detected during lactation, and it is crucial to know the pathogen present to select the appropriate cure. Overuse and misuse of antibiotics in treating bovine mastitis have led to problems in the dairy industry, and the cost of treatment is determined by the loss incurred due to milk discarded.[21]

Vaccination therapy:
Vaccinating cows is a preventive treatment for mastitis, targeting *Staph. aureus*, *Strep. agalactiae*, and *E. coli*. However, vaccines have not provided reliable protection. *Startvac*, a commercial vaccine, has shown moderate efficacy in reducing new infections and duration of mastitis, but was found ineffective in improving udder health, milk production, or survival. Mastitis is caused by various bacterial pathogens, and vaccination alone is not effective, especially in dairy herds with high mastitis rates. Vaccination must be combined with other control procedures like hygienic milking, antibiotic treatment, and infected cow culling. A vaccine that protects against multiple strains should be easily implementable and economically affordable.[22]

Potential Alternative Treatment:
Plants, rich in traditional medicine ingredients, are increasingly being studied for treating bovine mastitis due to their antimicrobial properties and low toxicity. Plant-derived compounds do not induce resistance and can inhibit inflammation caused by pathogens. Some of the plant extract with their mechanism of action are mentioned below in the table:

Table no1 : Plant extract with their Mechanism of action.

Plant Name Biological Source / Family	Comman Name	Chemical Constiteunt	Dosage Form	Activity
Aconitum plant /Ranunculaceae[23]	Wolfsbane	Aconitine	Oral Liquid	Analgesic and anti-inflammatory
Aloe barbadenis miller/liliaceae[24]	Aloe Vera	Aloin	Gel ointment or cream	Antioxidant and Antibacterial
Allium cepa/ Amaryllidaceae[25]	Onion	Allicin and Streptozotocin	Oral preparation	Antimicrobial and antiparasitic
Allium sativum/ Amaryllidaceae[25]	Garlic	Alliin and Allicin	Oral preparation	Antibacterial, antifungal and antitumoral
Atropabellodona/ Solanaceae[27]	Devil's cherries	Atropine and Scopolamine	Injection liquid	Muscle relaxant, Analgesic and Anti-inflammatory

Calendula officinalis/ Asteraceae[29]	Marigold	Heneicosane and Cadinol	Ointment or cream	Antifungal, antibacterial and healing wounds
Macrocystispyrifera/ Lessoniaceae[28]	Kelp	D-mannuronic acid and L-guluronic acid	Oral or sheets of cover infected area	Heals wound and other bleeding problems
Curcuma longa/ Zingiberaceae[26]	Turmeric	Curcumin and Curcuminiod	Cream, ointment and oral preparations	Antiseptic, antimicrobial, healing wounds and uneasiness
Trachyspermumammi/ Umbellifers[29]	Carumajwon	Thymol	Oral preparation	Antinociceptive, antispasmodic, Antimicrobial
Zingiberofficinale / Zingiberaceae[26]	Ginger	Gingerol and beta-sesquiphellandrene	Oral preparation	Antimicrobial and broad spectrum activity

In summary, herbal medicines contain bioactive components with great value in preventing and treating bovine mastitis, with mechanisms of action similar to antibiotics, but without the presence of antibiotic residues in milk

PREVENTION

It is preferable to stop mastitis before it causes issues. The following actions can greatly aid in prevention:

- Give cows enough bedding that is clean, dry, and sufficient to rest on.
- It is important for cows to be clean when they approach the milking area.
- Each cow's teats should be cleaned with a different cloth or paper towel before milking.
- After milking, use teat dips containing germicidal agents.
- Finally, feed the cows so they don't collapse right away. This keeps germs from entering teat canals while they are still open during milking.

REFERENCES

[1]. OIE (2008): Guidelines on the responsible and prudent use of antimicrobial agents in veterinary medicine,:http://www.oie.int/eng/normes/Mcode/ en_chapitre_1.6.7.htm June 1/2016].
[2]. Mukasa-Mugerwa, E. (1998): Review of reproductive performance in female Bas indicus (Zebu) cattle. ILCA monograph, No.6.ILCA, Addis Ababa
[3]. Gomes F, Henriques M. Control of bovine mastitis: old and recent therapeutic approaches. *CurrMicrobiol.* 2016; 72:377–82. doi: 10.1007/s00284-015-0958-8. [PubMed] [CrossRef] [Google Scholar]
[4]. Hogeveen H, Steeneveld W, Wolf CA. Production diseases reduce the efficiency of dairy production: A review of the results, methods, and approaches regarding the economics of mastitis. *Annu Rev Resour Economics.* 2019; 11:289–312. doi: 10.1146/annurev-resource-100518-093954. [CrossRef] [Google Scholar]
[5]. Zhao X, Lacasse P. Mammary tissue damage during bovine mastitis: causes and control. *J Anim Sci.* 2008;86:57–65. doi: 10.2527/jas.2007-0302. [PubMed] [CrossRef] [Google Scholar]
[6]. Radostits, O. M., Gay, C. C., Blood, D.C. and Hinchcliff, K .W. (2000). Mastitis. In: Veterinary Medicine, 9th ed., W.B. Saunders Company Ltd., London, pp. 603-687.
[7]. Sears, P.M., R.N.Gonzalez, D.J. Wilson and H.R. Han (1993): Procedures for mastitis diagnosis and control.Vet.Clin.NorthAm.*FoodAnm.Practice***9**:445-468.
[8]. Guidry, A.J. (2007): Mastitis and the immune system of the mammary gland. In: *Lactation*. Larson, B.L. (eds). The Iowa State University Press, Ames, Iowa, USA. Pp. 229-262.
[9]. Heeschen, W.H. (2012): Introduction In: Monograph on the Significance of Microorganism in Raw Milk. International dairy federation. Wolf passing, Austria. Pp. 19-26.
[10]. Brown, J. L. (2006): A Survey of Food borne Pathogens in Bulk Tank Milk and Raw Milk Consumption among Farm Families in Pennsylvania. *J. Dairy Sci*., 89: 2451-2458.
[11]. Jones, G. M., R. E. Pearson, G. A. Clabaugh, and C. W. Heald (1984): Relationships between somatic cell counts and milk production. J. Dairy Sci. 67:1823-1831.
[12]. Makovec, J.A. &Ruegg, P.L. (2003): Results of milk samples submitted for microbiological examination in Wisconsin from 1994 to 2001. *Journal of Dairy Science*, 86, 3466–3472.
[13]. Dohoo, I.R., & Leslie, K.E. (1991): Evaluation of changes in somatic cell counts as indicators of new intramammary infections. *Preventive Veterinary Medicine* 10(3):225–237 .
[14]. Shaheen M, Tantary H, Nabi S. A treatise on bovine mastitis: disease and disease economics, etiological basis, risk factors, impact on human health, therapeutic management, prevention and control strategy. *Adv Dairy Res.* 2016; 4:1. doi: 10.4172/2329-888X.1000150. [CrossRef] [Google Scholar]
[15]. Myllys V., 1 995. Staphylococci in heifer's mastitis before and after parturition. J. Dairy Res. 62, 51–60.
[16]. Gurjar A., G. Gioia, Y. Schukken, F. Welcome, R. Zadoks and P. Moroni. (2012): Molecular diagnostics applied to mastitis problems on dairy farms. Vet. Clin. North Am. Food Anim. Pract. 28:565-576.

[17]. Zadoks, R.N., J.R. Middleton, S. McDougall, J. Katholm and Y.H. Schukken. (2011): Molecular epidemiology mastitis pathogens of dairy cattle and comparative relevance to humans. J. Mammary Gland Biol.Neoplasia. 16:357-372.
[18]. Wagner, S. and Erskine, R. (2006): Antimicrobial drug use in bovine mastitis. In: Antimicrobial Therapy in Veterinary Medicine 4th edn). Giguere S, Prescott JD, Baggot RD. (eds). Oxford, Blackwell. 768.
[19]. Watts, J. L. (2002): Etiological agents of bovine mastitis.*Veterinary Microbiology*. 16(1):41–66
[20]. Schukken Y., Wilson D., Welcome F., Garrison-Tikofsky L., Gonzalez R., Gonzalez Moni R., Schukken Y.H., Wilson D.J., Garrison-tikofsky L., Gonzalez R.N. Monitoring Udder Health and Milk Quality Using Somatic Cell Counts. *Vet. Res.* 2003;34:579–596. doi: 10.1051/vetres:2003028. [PubMed] [CrossRef] [Google Scholar]
[21]. Schukken Y., Wilson D., Welcome F., Garrison-Tikofsky L., Gonzalez R., Gonzalez Moni R., Schukken Y.H., Wilson D.J., Garrison-tikofsky L., Gonzalez R.N. Monitoring Udder Health and Milk Quality Using Somatic Cell Counts. *Vet. Res.* 2003;34:579–596. doi: 10.1051/vetres:2003028. [PubMed] [CrossRef] [Google Scholar]
[22]. Loy J.D., Clawson M.L., Adkins P.R.F., Middleton J.R. Current and Emerging Diagnostic Approaches to Bacterial Diseases of Ruminants. *Vet. Clin. N. Am. Food Anim. Pract.* 2023;39:93–114. doi: 10.1016/j.cvfa.2022.10.006. [PubMed] [CrossRef] [Google Scholar].
[23]. Eskinazi D. Homeopathy re-revisited: is homeopathy compatible with biomedical observations? Arch Intern Med. 1999;159:1981–7. - PubMed
[24]. Coats, B.C., R.E. Holland and R. Ahola. 1985. Creatures in our care: the veterinary uses of aloe vera. Published by the authors. 299 pages.
[25]. C. J. Cavallito and J. H. Bailey, "Allicin, the antibacterial principle of Allium sativum. I. Isolation, physical properties and antibacterial action," *Journal of the American Chemical Society*, vol. 66, no. 11, pp. 1950–1951, 1944.Google Scholar
[26]. M. Poeloengan, "The effect of red ginger (*Zingiberofficinale* Roscoe) extract on the growth of mastitis causing bacterial isolates," *African Journal of Microbiology Research*, vol. 5, no. 4, pp. 382–389, 2011.Google Scholar
[27]. MacLeod, G. 1981. The treatment of cattle by homeopathy. Health Science Press, Saffron Walden, Essex, England. 148 pages
[28]. Vacca, D.D. and R.A. Walsh. 1954. The antibacterial activity of an extract obtained from Ascophyllumnodosum. Journal of the American Pharmaceutical Association, 43 :24-26.
[29]. Jost, M. 1984. Calendula as a healing plant for mastitis in dairy cows. Biodynamics, No. 152:7-19.