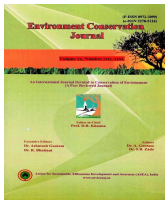
Environment Conservation Journal 24 (4): 335-343, 2023

Journal homepage: https://www.environcj.in/

Environment Conservation Journal

ISSN 0972-3099 (Print) 2278-5124 (Online)



Herbal treatment as an alternative to antibiotics for bovine mastitis in the system of obtaining environmentally safe milk

Ankita
Department of Microbiology, SGRR School of basic and applied sciences, Shri Guru Ram Rai University, Dehradun (U.K.), India
Shrishti Raturi
Department of Microbiology, SGRR School of basic and applied sciences, Shri Guru Ram Rai University, Dehradun (U.K.), India.
Manjusha Tyagi ✉
Department of Microbiology, SGRR School of basic and applied sciences, Shri Guru Ram Rai University, Dehradun (U.K.), India.

ARTICLE INFO

Received : 15 March 2023
Revised : 20 June 2023
Accepted : 04 July 2023

Available online: 18 October 2023

Key Words:
Antibacterial
Antibiotic
antibiotic resistance
California mastitis test (CMT)
cardiovascular disease
somatic cell
veterinary

ABSTRACT

Antibiotics are known as the first option for treating any disease. While, the difficulty in terms of antimicrobial resistance and antibiotic residue as well as antibiotic impact is application on health of the public, results in numerous limitations on unregulated antibiotic treatment worldwide within the dairy industry. Scientists looked into new healing strategies that could be used to replace antibiotic use in mastitis disease treatment. Bovine mastitis causing a direct impact on food safety issues and the farm's profitability. This pathology's treatments and preventions are specially performed using antimicrobials, However, this disease's pathogens' increasing antimicrobial resistance may have an impact on the customary drug's effectiveness. Moreover, the environment and the presence of antimicrobial residues in milk are a probable danger in terms of human health. As a result, the utilization of plant extracts could become a hopeful alternative for bovine mastitis prevention. Antibacterial properties are included in numerous plants. Plants extracts are usually considered secure for animals, humans, and the environment. This analysis contains the common issues that came across in the customary Mastitis Treatment, including the potential uses of plant extracts as substitutes for the control of these pathogens, as well as the constraints of using these plant derivatives.

Introduction

Milk is as old as mammals. Milk is the most many-sided product in the food industry. It gives us balanced nutrition from birth until the time when we can eat solid feeds. It is supposed that ancient people discovered domesticating animals for the production of milk for human consumption. They domesticated animals like animals such as cows, buffaloes, goats, sheep, and camels. Some of these creatures are still in use for milk production in numerous regions of the world. Beyond milk, financial relevance, and milkproducts are essential in the human diet because a source of micro and macronutrients (Akin, 2018), imparting proteins, potassium, calcium, vitamin D, vitamin B12, riboflavins, fatty acids, as well as phosphorus (Keast *et al.,* 2013), (O'Neil *et al.,* 2018), (Quann *et al.,* 2015).The aforementioned items are consumed straight away. Accompanied by excellent skeletal well-being, mainly concerning kids as well as teenagers, and a reduced risk of hypertension, coronary artery disease (CAD), and non-insulin-dependent diabetes mellitus (NIDDM) in adults.To get milk of superior quality, perfect health of the udder is not solely necessary only in support of the dairy producer, However, it is also applicable to the entire chain of manufacturing for dairy products (Hogeveen *et al.,* 2011). Moreover, enhancing directed heightened public knowledge and government oversight focus towards the security and integrity of food troubles emphasize the importance of the sector of dairy production taking proactive measureswith the purpose of denoting and laying off new food safety concerns that may arise representing a negative influence on the

Corresponding author E-mail: *manjushatyagi2008@gmail.com*
Doi: https://doi.org/10.36953/ECJ.25762721

perception of dairy products (Boor *et al.,* 2001). Pathogens of udder control can minimize foodborne diseases and offer nutritious food to consumers that is safer and of superior quality (Bajpai *et al.,* 2013). Because of public health concerns reasons, antibiotic residues, and microbial resistance allied with the dairy swarm, Agriculture animals must alertly investigate the use of antimicrobials and implement exemplary stewardship procedures structured to decrease the danger of creating recently discovered bacteria that are resistant to antibiotics that could be passed to humans from animals (Foutz*et al.,* 2018).The financial growth pertaining to the dairy industry prompts research into increasing food safety and environmental production that is long-term. As a result of this standpoint,plant extract utilization could be a promising artificial drug substitute. The purpose of this review contains to go over the utilization of a collection of extracts from plants asa substitute for mastitis dairy cattle control, with an emphasis in terms offuture tendencies and potential implications for the application of suchproducts in the veterinary field. Bovine mastitis results inyearlyfinancial losses of approximately $35 billion worldwide and in the United States of America is $2 billion (Mubarack HM *et al.,* 2011). Mastitis is known asthet cost-effective diseaseinthe dairy industry, affecting both highly developed and developing countries. Mastitis has an impact on milk quality, and its consequences extend beyond the dairy farm. Consumer concerns about milk quality, antimicrobial resistance, antimicrobial residues, and animal welfare necessitate the development of appropriate policies for effective prevention and mastitis control. Because of the permanent damage that mastitis can cause to the mammary secretory tissues, the loss of production of milk is not limited to the course of the disease but may continue throughout the animal's life.

Antibiotic treatment disadvantages in mastitis

Several studies in recent years have found that mastitis pathogens are developing antimicrobial resistance and that conventional treatments have low cure rates (Freitas *et al.,*2018). Bacterial resistance mechanisms are very versatile, and they are influenced by whether a population has resistant variants, whether there are differences in reproductive successoccurringwhen antibiotics are present, and whether the variation is inherited. According tosuch cases, the composition of the population will shift in support of resistant strains over time (Baquero, 2011). During the lactation period when antimicrobials are administered, As a result of the high danger of residues of drugs, milk must be discarded for an extended period, posing a possible danger to human well-being. These leftovers may be harmful to antimicrobial-sensitive consumers, encourage bacterial immunity, and impede the production of derived products of milk (Blowey and Edmondson, 2010). Long-acting antibiotics can be used to treat the cows, however, milk from these types of cows cannot be sold until the residues of the drug have passed through the system ofthe cows. If the levels of antibiotic residuals in milk are high, milk should be siphoned off and discarded. The UK government convened a meeting on the global situation of antibiotic resistance in 2014, as well as a subsequent impact assessment's performance. To keep antibiotics effective both humans and animals can benefit from this therapeutic measure., both veterinary and human medicine sectors must limit the development of resistance and take responsibility. The current study sought to investigate the occurrence of mastitis resistant to medication and antibiotic resistance patterns in dairy cows. Humans have been exposed to Staphylococcus aureus resistant to methicillin (MRSA) strains by animals, but this transmission's epidemiology is unknown (Juhász-Kaszanyitzky *et al.,* 2007). Regardless of the results of in vitro tests, MRSA should be taken into account as resistant topenicillin, cephems, cephalosporins, as well as other beta-lactam antibiotics like ampicillin-sulbactam, ticarcillin-clavulanic acid, piperacillin-tazobactam, amoxicillin-clavulanic acid, and carbapenems. (CLSI, 1997). Antimicrobial agents that are most commonly used such as aminoglycosides, tetracycline macrolides, chloramphenicol, and fluoroquinolones are also frequently resistant to these organisms (Clinical and Laboratory Standards Institute, 2006), (Türkyılmaz *et al.,* 2010). Antimicrobial therapy is commonly used to prevent and treat mastitis. Unfortunately, despite the most effective antimicrobial therapies available, bacteriological treatment failures are quite common, especially in the case of antimicrobial resistance and mastitis which is thought to be among the causes of a low rate of cure (Barkema *et*

al., 2006). Antimicrobial resistance bacteria are a public health risk. Several strains of *Staphylococcus aureus* isolated from mastitis patients are resistant to a variety of antimicrobials, including penicillin-G, ciprofloxacin, streptomycin, gentamicin, ampicillin, and oxytetracycline (Kumar *et al.,* 2011).

Plant extracts used as alternative treatments for bovine mastitis

Some plants, also known as medicinal plants, may be used for therapeutic purposes. Chemical compounds are found in these plants that have beneficial biological properties for the benefit of animal and human health (Paz *et al.,* 2018). Lately,promising experimental findings by the utilization derived from botanical sources with medicinal properties havegiven the stimulus for bioactive substance research and the possibility of new products. All plants generate primary metabolites, Amino acids, fatty acids, carbohydrates, and organic acids are examples, which are required to survive (Tian *et al.,* 2018). Bioactive compounds, in contrast, occur in lower amount and usually necessary to the defenses of plants (for example, causing bitter formation, substances that are detergent, toxic, or pungent) guarding them against the majority of Herbivores, microorganisms, and plants that compete for resources are all examples of herbivores directly. These metabolites were potentially derived through plant extracts, which are preparations with varying consistency as well as compositions (GouveaFD, *et al.,* 2017),that seek to extract as well aspurification of bioactive compounds by botanical species matter (Tan *et al.,* 2013).

Maceration, digestion, percolation, infusion, and decoction, Soxhlet hot uninterrupted retrieval, fermentation extraction with a water-alcohol solution, microwave assisted solvent extraction, supercritical fluid based extraction, counter-current and ultrasonic extraction, as well as distillation methods are all used to obtain those extracts (Pandey and Tripathi, 2014). among the older methods based onorganic solvent extraction is the hot continuous extraction process, where the sample comes inat a distance from the solvent comparatively moreheat level (Ghaderi and Ebrahimi, 2015). Solvents permeate within the solid materials ofthe nt during the process and make the compounds more soluble with comparable polarities (Pandey and Tripathi, 2014), the elimination process will follow. Also, extraction with the assistance of ultrasonic waves employs dissolving agents and is superior to the more conventional proceduresbecause of its high effectiveness, lower solvent volume requirements, andshort period of extraction. (Macías-Sánchez *et al.,* 2009). Supercritical fluid extraction, alternatively, is a widely used procedure that makes use of supercritical fluids (above-critical-point temperature and pressure) and offers benefits such as increased selectivity and lower temperatures, staying away from Solvents and thermal degradation that remain. The most significant disadvantage of fluid that is supercritical is the more advanced equipment cost needed for extraction when in comparison to conventional extraction of dissolving agents (Yen *et al.,* 2015).To address the issue of bacterial resistance caused by the continued antibiotic usage in dairy herds, exploration into complementary therapiesis increasing. The specified types of therapies, which primarily make utilization of extracts of plants, are effective In vitro control of pathogens that cause mastitis. Natural occurrence, feweradverse effects (Khe*et al.,* 2018) as well as a lack of resistance that develops following extended (Montironi*et al.,* 2016).These compounds have a significant advantage over conventional drugs. Indeed, numerous Several studies have confirmed the effectiveness as a result of these plant derivatives. For example, Extracts of *Azadirachta indica* leaves exhibitthe properties of bactericidal power.It is now underway to have substantial influences on gram-positive and also on gram-negative pathogens as well as additional bacterial species responsible for a variety of illness affecting both humans and animals(Maragathavalli*et al.,* 2012).

Some major losses due to mastitis

Milk must be discarded during treatment days and waiting periods due to the treatment of a clinical case. In general, milk is assumed to have been discarded for six days: three days of treatment and 3 days of rest(Huijps*et al.,* 2008). The treatment's costis also a significant factor to consider. The cost of treatment is divided into two parts: veterinarian fees and drug costs.These two costs vary by country. Labor costs calculation is difficult.Farm to

Figure 1: Neem leaves

farm, labor opportunity costs may vary. farm to farm. If labor is external, the time spenton labor costs preventing mastitis is simple to compute (hourly wage). In contrast, if labororiginated with the farmer, It is worth noting that mastitis may cause Farmers should not to spend as much time on administrative tasks. (Halasa *et al.,* 2007).Poor milk quality, premature cow culling,oranimals with a shorter productive life.The losses can be either temporary or permanent.The disease is clinically or subclinically classified based on the specific form of clinical symptoms. Clinical mastitis is distinguished byvisible symptoms like milk clots, and Teats with hardness and swelling (Blowey and Edmondson, 2010) recognized through a visual examination and manual exploration (Sadek*et al.,* 2016).There are no externally visible changes. in a subclinical infection (Blowey and Edmondson, 2010) and Auxiliary examinations, for instance, the California Mastitis Test (CMT) or somatic cell count examination in the laboratory are used to make the diagnosis (Sadek*et al.,* 2016).Mastitis has an impact on milk quality goes outside of the dairy farm. Consumer concerns about residues of antimicrobials, resistance to antimicrobial agents, animal welfare, and milk quality necessitate the development of appropriate policies for effective mastitis prevention and treatment. Because of the permanent damage that mastitis can cause to the mammary secretory tissues, the loss of production of milk is not limited to the disease progression but may continue throughout the animal's life. Histological analyses were and continue to be widely used for determining mastitis pathogen-induced damage to secretory tissue in the bovine mammary gland (Benites *et al.,* 2002). An inflammatory response was detected in 96.9% of the samples. (edema, damage to mammary epithelial cells, and Infiltration of polymorphonuclear neutrophils), procedure for tissue repair, or both in dairy cow's mammary parenchyma from which microorganisms were isolated. At the same time, there were no histological changes in mammary glands with no evidence of microorganisms. These findings clearly show that the presence of microorganisms is linked to tissue harm. All at once, it should be noted that Because of pain and decreased movement, inflammation can cause a decrease in appetite and food intake which will hurt milk production. Many methods have been developed to compute the losses of production caused by Dairy cow mastitis. Neither of the methods are ideal because it is impossible to know how much milk a cow would have produced if lactation had not been interrupted by mastitis. Every technique has an inherent prejudice that, in the majority of cases, tends to understate the actual loss of milk production.Nonetheless, scientists agree that milk yield losses are the primary economic impact of subclinical mastitis (Schepers and Dijkhuizen, 1991).It was discovered that the sole item in all previous papers' estimates examined that was concerned with the Mastitis economics was a change in milk production.Estimates of milk yield loss continue to be a source of concern because they are most likely influenced by age, cow breed and type, udder's morphological characteristics s, and lactation stage, Before mastitis, milk yield was higher, organisms that cause mastitis, grade of inflammation, Early or late post-occurrence diagnosis, treatment type, feeding procedures, season, Mastitis recurrence during the same lactation or earlier, model of comparison (control group), and Some mastitis causal agents, for example, have been demonstrated to have a greater impact on the yield of milk than others. In general, the more inflammation there is, the less milk is produced (Petrovski *et al.,* 2006). Using the performance of an infected quarter as a comparison to the performance of the uninfected quarter on the opposite side, it is generally acknowledged that the contralateral udder quarters produce roughly the same amount of milk when both are uninfected. Simultaneously, this is scientific proof that quarter are s that mastitis-freemay make up for mastitis-infected quarters by boosting milk production. If

there is compensation occurs, the actual milk loss due to mastitis will be overestimated.(Petrovski*et al.,* 2006)

Transmission

Contact with the milking machine regularly, as well as contaminated materials or hands, transmission from mouth to udder among calves. The mastitis-causing bacteria strain will remain dormant in the calf's oral cavity until it is transmitted elsewhere, In a muddy, wet condition, with Inadequate milking techniques and hygiene.Mastitis is a multifactorial disease caused by the interaction betweenseveral parameters including the host, pathogens, management, as well as the environment. Mastitis is caused through a diverse range of etiological agents, incorporating a significant multitide of microorganisms that cause udder inflammation. Bacterial pathogens are the most dangerous infectious agents to the breast gland. They are frequently contagious and widespread in an environment of dairy animals and thus raise the rate of occurrence of intramammary infections. Infection is caused by either contaminated environments or infected udders. Pathogens are spread primarily through contaminated quarters and soiled udders, milking machines that have become contaminated, flies, washing clothes milker's hands, tea cups, and surgical instruments. Furthermore, lactation stage,lactations number, udder trauma, loose teat sphincters, teat, and teat canal, lesions on teat skin of each mammary gland's immunological status, the amount of contamination in the environment management conditions are among the factors that influence (Alemu *et al.,* 2013) the occurrence of mastitis in dairy animals.

Etiology

Mastitis etiological agents are classified divided into two: environmental and contagious. Contagious microorganisms typically reside in theteat skin or udderduring milking, they are transferred to the teat., where they multiply and as well as spread throughout mammary glands. Environmental agents, in contrast, survive in the environment of the cow and make their way into the udder via transportby teat canal for instance throughout milking, through the activity of capillaries, antibiotic administration of a tube, or teat cannula insertion) or teat canal indirect penetration quickly after the completion of milking (Scott *et al.,* 2011). While there maybe a few differences in how these microbes are classified. Transmissible pathogenic agents include *Staphylococcus aureus*,*Mycoplasma spp., Corynebacterium bovis*, *Streptococcus agalactiae*, and *Streptococcus dysgalactiae*, while environmental pathogens *Citrobacter spp*. is one of them, *Enterobacter spp*., *Klebsiella spp*., *Escherichia coli*, *Pasteurella spp*., (Blowey and Edmondson, 2010) Because of its potential to deliver a diverse set of pathogenic attributes that aid in bacterial intrusion. *Staphylococcus aureus* remains among the prevailing causative organism. (Saei, 2012), (Marques *et al*., 2017). Bovine intramammary infections can manifest as subclinical, acute, chronic, or toxic. resulting in significant monetary losses (Käppeli *et al*., 2019). *Staphylococcus aureus* is frequently regarded as the most significant microorganism linked to mastitis. This pathogen's intramammary infections are difficult to treat. Because They are vulnerable to recurrence and chronicity. (Peton*et al*.,2014). Mastitis can be caused by a traumatic or toxic event., but A microbiological infection is usually to blame according to The International Dairy Federation (ID A) (1987). In addition, over 150 different microorganisms that cause disease have been identified as mastitis-causing agents in dairy cows.Bacteria, fungi, and yeasts could all be involved,However, bacteria play by far the most important role. (Quinn *et al*., 2002).Although it is unknown what causes 20 to 35% of clinical mastitis cases.,(Wellenberg *et al.,* 2002) It is assumed bovine mastitis is primarily caused by bacteria. It can be either contagious or environmental.

Detection:California mastitis test (CMT):

CMT is anuncomplicated and reliable test for subclinical mastitis that can be applied universally. Its design was aimedat test milk from specificudder quarters as well as composite milk samples. To obtain reliable readings, recently collected milk and not refrigeratedcan be examined for a maximum of 12 hours, andThe CMT can test refrigerated milk for as long as 36 hours. The test helps to determine the level of infection occurring in every udder quarter as opposed to a total udder outcome andthe outcome onlyirrespective of the cell count is elevated or reduced is indicated. (CMT) is a straightforward indicator of milk's somatic cell

count (SCC). It works by introducing a reagent into the milk sample that disrupts the cell membrane of somatic cells. It is a simple but very effective technique that can be used by any member of the farm staff to provide an immediate result.

Somatic cell count:

Somatic Cell Count (SCC) is a significant milk quality determinant.Leukocytes constitute themost somatic cells (white blood cells) that are becoming increasingly common in milkas a defensivereaction against a mastitis-causing pathogen,in addition to a few glandular cellswhen an infection arises, these milk-secreting cells sloughed off from the udder's internal tissue.

Table 2: Scoring chart of california mastitis test

The number of leukocytes per milliliter	The appearance of the test	Score of CMT
Below 200,000	In the liquid mixture, there is no precipitation in the mixture.	Negative
150,000 to 500,000	The light precipitation dissipates with the movement of the paddle.	Slight
400,000 to 1,500,000	It distinct precipitate but does not blend with the movement of the paddle.	1
800,000 to 5,000,000	The formation of a gel is distinct.	2
Over 5,000,000	The formation of a strong gel that sticks to the paddle. It has a distinguishable central peak.	3

Flow cytometry (FC):

A methodofdeterminingcells' chemical and physical properties as they move in a state of suspension. past a sensing point. This method was recently created to quantifymilk somatic cell counts and it is especially useful in the detection of subclinical mastitis (Tian, 2005), (Holm, 2004)

Culture method:

Mastitis is most accurately diagnosed by identifying and isolatingany pathogenic microorganisms found in milk. This could be accomplished through Cultural methods, as well as a variety of additional determining tests.To obtain accurate results while avoiding contamination and, as a result, bias, it is critical to work safely as well as ina precise manneras much as possible given the circumstances (Quinn *et al*., 2002).

Vaccination

Mastitis vaccines are available, but they cannot prevent recurrent infections. There are several commercially available mastitis vaccines, however, neither of them provides adequate protection while also being cost-effective(Sharun*et al.,* 2021*)*.As a result of the multiple etiologies, no effective vaccine against all possible pathogens is available; however, various vaccines against bacterial pathogens have been attempted with mixed success. The insufficient protective potential may be due to a variety of variables, as well asthose pertaining to bovines. For instance health and age category, environment, or invading microorganism like elevated prevalence of pathogens that cause mastitisin spite of genetic differences within mastitis-causing genotypes from the same kind, as well as variations in individual animal immune responses based on genetic and environmental variables(Côté-Gravel and Malouin, 2019), (Merrill *et al*., 2019), (Scholte, 2019).

Control and prevention

The phrase "prevention is better than cure" perfectly describes the condition of mastitis. Mastitis can be reduced through better animal husbandry and better hygiene methods of the handling of animals (Kumar *et al.,* 2010*)* The majority of cases of bovine mastitis caused by udder damage, which then comeswith a microbial infection, these are avoidable, even if they occur by chance, treatment should be prompt as well as consistent. Pathogens enter primarily via open teat canals and animals with a high yield and a soft opening and teat canal closure is delayed during milking or milk dripping from teats as a result of delayed milking, which may bethe microbial invasion source bysoil, polluted water, or litter. All of these issues are manageable through good shed cleanliness and administration.The implementation of antiseptics after milking process and at the teat entrance reduces the possibility of microbial entry and is regarded as a successful management strategy fordisease avoidance (Olde *et al*., 2012). Bovine mastitis is always reduced when disinfectants are used on a consistent and timely basis in paddocks and the shed. Milk samples and regular milk screening always reducethe out of infected animals. Color and consistency observations, two milk-straining methods that are commonly used, increase the likelihood of detecting mastitis early. Breeding, control of flies,

proper nutrition, improved milking sanitation, prevention of cross-sucking among young children, use of procedures for disinfecting teats after milking, routinely inspection of milking equipment, and use of milking sequence, and bedding material enhancement are all measures aimed at preventing new mastitis cases (Shkreta *et al.,* 2004), (Calzolari *et al.* 1997*),*(Fontaine *et al*., 2002), (Chang *et al*., 2008), (Nielsen, 2009), (Yin et *al.,* 2009), (Vliegher *et al*., 2012).

Conclusion

A worldwide trend towards greater environmental sensitivity in farm animal management is currently being driven by increased Concerns about public health and consumer acceptance. Because pathogens have high levels of antibiotic resistance, alternative treatments for bovine mastitis are urgently needed. Plant derivatives hold great promise as a source of new antimicrobial agents., demonstrating efficacy against resistant microorganisms in vitro and, in some instances, in vivo, and are thought to be less harmful to plants, animals, and the environment. Bacteria have devised complex mechanisms to avoid antibiotic attacksand survive, which is a procedure that is accelerated most likely by heightened utilization of antimicrobials. Insusceptible to antibiotics has arisen as one of the most serious dangers to public health twenty-first century. To design novel anti-threat strategies, knowledge of the ways in which bacteriawhich bacteria developresistance to antibiotics is required. As a result, Antimicrobial drug development efforts andresearch resistance mechanisms must be ongoing to reduce the issue. Mastitis is a problematic condition that is currently one of the most serious conditions that cause damage in the dairy business. The financial losses caused by the circumstances are irreparable, as a result of the late misdiagnosis of the primary agent responsible for the etiology. Diagnosis failure is primarily due to disease complicity.

Acknowledgement

The authors would like to convey their appreciation to the Professor and Head Department of Microbiology at Shri Guru Ram Rai University Dehradun, Uttarakhand, for his assistance in various ways throughout this study.

Conflict of interest

The authors declare that they have no conflict of interest.

References

Akin, I., Akin, T., (2018). Economic impact of digital dermatitis treatment on a dairy farm: an application of the break-even analysis. Cienc. Rural. 48, e20170791.

Alemu LA, Melese AY, Gulelat DH (2013). Effect of endogenous factors on proximate composition of nile tilapia (Oreochromis niloticus L.) fillet from lake zeway. *American Journal of Research Communication.* 1(11):405-10.

Bajpai, V.K., Sharma, A., Baek, K.H., (2013). Antibacterial mode of action of Cudraniatricuspidata fruit essential oil, affecting membrane permeability and surface characteristics of food-borne pathogens. *Food Control* 32, 582–590.

Baquero, F., (2011). The 2010 Garrod lecture: the dimensions of evolution in antibiotic resistance: ex unibusplurum et ex pluribus unum. *J. Antimicrob. Chemothe. 66*, 1659–1672.

Barkema, H.W., Schukken, Y.H. and Zadoks, R.N. (2006) Invited review: The role of cow, pathogen, and treatment regimen in the therapeutic success of bovine Staphylococcus aureus mastitis. 89: 1877–1895

Benites NR, Guerra JL, Melville PA, Da Costa EO (2002). Aetiology and histopathology of bovine mastitis of espontaneous occurrence. *Journal of Veterinary Medicine*, Series B.Oct;49(8):366-70.

Blowey, R., Edmondson, P., (2010). Mastitis Control in Dairy Herds, second ed. Cabi, Wallingford.

Boor, K.J., (2001). Fluid dairy product quality and safety: looking to the future. *J. Dairy Sci*. 84, 1–11.

Calzolari, A., J.A. Giraudo, H. Rampone, L. Odierno and A.T. Giraudo *et al*., (1997). Field trials of a vaccine against bovine mastitis. 2. Evaluation in two commercial dairy herds. *J. Dairy Sci*., 80: 854-858.

Chang, B.S., J.S. Moon, H.M. Kang, Y.I. Kim and H.K. Lee *et al*., (2008). Protective effects of recombinant staphylococcal enterotoxin type C mutant vaccine against experimental bovine infection by a strain of *Staphylococcus aureus* isolated from subclinical mastitis in dairy cattle. Vaccine, 26: 2081-2091.

Clinical and Laboratory Standards Institute, (2006). Performance Standards for Antimicrobial Susceptibility

Testing; Sixteenth Informational Supplement. CLSI document M100-S16. CLSI, Wayne, PA.

Côté-Gravel, J., and Malouin, F., (2019). Symposium review: Features of Staphylococcus aureus mastitis pathogenesis that guide vaccine development strategies, *Journal of dairy science,* 102, 4727-4740

De Vliegher, S., L.K. Fox, S. Piepers, S. McDougall and H.W. Barkema, (2012). Invited review: Mastitis in dairy heifers: Nature of the disease, potential impact, prevention and control. *J. Dairy Sci.*, 95: 1025-1040.

Fontaine, M.C., J. Perez-Casal, X.M. Song, J. Shelford, P.J. Willson and A.A. Potter, (2002). Immunisation of dairy cattle with recombinant *Streptococcus uberis* GapC or a chimeric CAMP antigen confers protection against heterologous bacterial challenge. Vaccine, 20: 2278-2286

Foutz, C.A., Godden, S.M., Bender, J.B., Diez-Gonzalez, F., Akhtar, M., Vatulin, A., (2018). Exposure to antimicrobials through the milk diet or systemic therapy is associated with a transient increase in antimicrobial resistance in fecal Escherichia coli of dairy calves. *J. Dairy Sci*. 101, 10126–10141.

Freitas, C.H., Mendes, J.F., Villarreal, P.V., Santos, P.R., Gonçalves, C.L., Gonzales, H.L., Nascente, P.S., (2018). Identification and antimicrobial susceptibility profile of bacteria causing bovine mastitis from dairy farms in Pelotas, Rio Grande do Sul. Braz. J. Biol. 78, 661–666.

Ghaderi, A., Ebrahimi, B., (2015). Soxhlet extraction and gas chromatography mass spectrometry analysis of extracted oil from Pistaciaatlanticakurdica nuts and optimization of process using factorial design of experiments. *Sci. J. Analyt. Chem.* 3, 122–126.

Gouvea FD, Rosenthal A, Ferreira EH (2007). Plant extract and essential oils added as antimicrobials to cheeses: a review. Ciência Rural. Jun 22;47.

Halasa T, Huijps K, Østerås O, Hogeveen H (2007). Economic effects of bovine mastitis and mastitis management: A review. Veterinary quarterly.Jan 1;29(1):18-31.

Hogeveen, H., Huijps, K., Lam, T.J.G.M., (2011). Economic aspects of mastitis: new developments. N. Z. Vet. J. 59, 16–23.

Holm H (2004). Gorenstein homological dimensions. *Journal of pure and applied algebra*. May 1;189(1-3):167-93.

Huijps K, Lam TJ, Hogeveen H (2008). Costs of mastitis: facts and perception. *Journal of Dairy Research*.Feb;75(1):113-20.

Juhász-Kaszanyitzky, É., Jánosi, S., Somogyi, P., Dán, Á., Bloois, L., Duijkeren, E., Wagenaar, J.A., (2007). MRSA transmission between cows and humans. Emerg. Infect. Dis. 13, 630–632.

Käppeli, N., Morach, M., Corti, S., Eicher, C., Stephan, R., Johler, S., (2019). Staphylococcus aureus related to bovine mastitis in Switzerland: clonal diversity, virulence gene profiles, and antimicrobial resistance of isolates collected throughout (2017). *J. Dairy Sci*. 102, 3274–3281

Keast, D.R., Fulgoni, V.L.I.I.I., Nicklas, T.A., O'Neil, C.E., (2013). Food sources of energy and nutrients among children in the United States: National Health and nutrition examination survey 2003–2006. *Nutrients* 5, 283–301.

Kher, M.N., Sheth, N.R., Bhatt, V.D., (2018). In vitro antibacterial evaluation of Terminalia chebula as an alternative of antibiotics against bovine subclinical mastitis. *Anim. Biotechnol*. 1–8.

Kumar, A., A. Rahal, S.K. Dwivedi and M.K. Gupta, (2010). Bacterial prevalence and antibiotic resistance profile from bovine mastitis in Mathura, India. Egypt. *J. Dairy Sci*., 38: 31-34

Kumar, R., Yadav, B.R. and Singh, R.S. (2011) Antibiotic resistance and pathogenicity factors in Staphylococcus aureus isolated from mastitic Sahiwal cattle. *J. Bio. Sci*. 36: 175-188

Macías-Sánchez, M.D., Mantell, C., Rodríguez, M., de la Ossa, E.M., Lubián, L.M., Montero, O., (2009). Comparison of supercritical fluid and ultrasound-assisted extraction of carotenoids and chlorophyll a from Dunaliellasalina. Talanta 77, 948–952.

Maragathavalli S, Brindha S, Kaviyarasi NS (2012). Antimicrobial activity in leaf extract of Neem (Azadirachtaindicalinn.). *International journal of science and nature*. 3(1): 110–3.

Marques, V.F., da Motta, C.C., Soares, B., Melo, D.A., Coelho, S., Coelho, I., Barbosa, H.S., Souza, M.M.S., (2017). Biofilm production and beta-lactamic resistance in Brazilian Staphylococcus aureus isolates from bovine mastitis. *Braz. J. Microbiol*. 48, 118–124.

Merrill, C., Ensermu, D., Abdi, R., Gillespie, B., Vaughn, J., Headrick, S., Hash, K., Walker, T., Stone, E., and Dego, O.K., (2019). Immunological responses and evaluation of the protection in dairy cows vaccinated with staphylococcal surface proteins, *Veterinary immunology and immunopathology*, 214, 109890

Montironi, I.D., Cariddi, L.N., Reinoso, E.B., (2016). Evaluation of the antimicrobial efficacy of Minthostachysverticillata essential oil and limonene against Streptococcus uberis strains isolated from bovine mastitis. *Rev. Argent. Microbiol*. 48, 210–216

Mubarack HM, Doss A, Dhanabalan R, Venkataswamy R (2011). Activity of some selected medicinal plant extracts against bovine mastitis pathogens. *J. Anim. Vet. Adv*. Jan 1;10(6):738-41.

Nielsen, C., (2009). Economic impact of mastitis in dairy cows. Ph.D. Thesis, Swedish University of Agricultural Sciences Uppsala, Sweden.

O'Neil, C.E., Nicklas, T.A., Fulgoni III, V.L., (2018). Food sources of energy and nutrients of public health concern and nutrients to limit with a focus on milk and other dairy foods in children 2 to 18 years of age: national health and nutrition examination survey, 2011–2014. *Nutrients* 10, 1–37

Olde Riekerink, R.G.M., I. Ohnstad, B. van Santen and H.W. Barkema, (2012). Effect of an automated dipping and backflushing system on somatic cell counts. *J. Dairy Sci*., 95: 4931-4938.

Pandey, A., Tripathi, S., (2014). Concept of standardization, extraction and pre phytochemical screening strategies for herbal drug. *J. Pharmacogn. Phytochem*. 2, 115–119.

Paz, J.E.W., Contreras, C.R., Munguía, A.R., Aguilar, C.N., Inungaray, M.L.C., (2018). Phenolic content and antibacterial activity of extracts of Hamelia patens obtained by different extraction methods. *Braz. J. Microbiol.* 49, 656–661.

Peton, V., Le Loir, Y., (2014). Staphylococcus aureus in veterinary medicine. Infect. Genet. Evol. 21, 602–615.

Petrovski KR, Trajcev M, Buneski G (2006). A review of the factors affecting the costs of bovine mastitis. *Journal of the South African Veterinary Association*. Jun 1;77(2):52-60.

Quann, E.E., Fulgori III, V.L., Auestad, N., (2015). Consuming the daily recommended amounts of dairy products would reduce the prevalence of inadequate micronutrient intakes in the United States: diet modeling study based on NHANES 2007–2010. *Nutr. J*. 14, 1–11.

Quinn, P.J. Carter, M.E. Markey, B. K. and Carter, G. R. (2002): Veterinary Microbiology and Microbial Diseases, Bacterial Causes of Bovine Mastitis, 8th Edition, Mosby International Limited, London, pp. 465 475.

Sadek, K., Saleh, E., Ayoub, M., (2016). Selective, reliable blood and milk bio-markers for diagnosing clinical and subclinical bovine mastitis. *Trop. Anim. Health Prod*. 49, 431–437.

Saei, H.D., (2012). Coa types and antimicrobial resistance profile of Staphylococcus aureus isolates from cases of bovine mastitis. *Comp. Clin. Path*. 21, 301–307.

Schepers JA, Dijkhuizen AA (1991). The economics of mastitis and mastitis control in dairy cattle: a critical analysis of estimates published since 1970. *Preventive Veterinary Medicine*.Mar 1;10(3):213-24.

Scholte, C.M., (2019). Antibiotic Alternatives for Treatment of Mastitis in Dairy Cattle

Scott, P.R., Penny, C.D., Macrae, A.I., (2011). Cattle Medicine, first ed. Manson Publishing Ltd, London, pp. 216–218.

Sharun, K., Dhama, K., Tiwari, R., Gugjoo, M.B., Iqbal Yatoo, M., Patel, S.K., Pathak, M., Karthik, K., Khurana, S.K., Singh, R., Puvvala, B., Amarpal, Singh, R., Singh, K.P., and Chaicumpa, W., (2021). Advances in therapeutic and managemental approaches of bovine mastitis: A comprehensive review, Veterinary Quarterly, 1-58

Shkreta, L., B.G. Talbot, M.S. Diarra and P. Lacasse, (2004). Immune responses to a DNA/protein vaccination strategy against *Staphylococcus aureus* induced mastitis in dairy cows. Vaccine, 23: 114-126.

Tan, M.C., Tan, C.P., Ho, C.W., (2013). Effects of extraction solvent system, time and temperature on total phenolic content of henna (Lawsoniainermis) stems. *Int. Food Res. J*. 20, 3117–3123.

Tian L (2005). Inferences on the common coefficient of variation. Statistics in medicine. Jul 30;24(14):2213-20.

Tian, M., Xu, X., Liu, F., Fan, X., Pan, S., (2018). Untargeted metabolomics reveals predominant alterations in primary metabolites of broccoli sprouts in response to preharvest selenium treatment. Food Res. Int. 111, 205–211.

Türkyılmaz, S., Tekbıyık, S., Oryasin, E., Bozdogan, B., (2010). Molecular epidemiology and antimicrobial resistance mechanisms of methicillin-resistant Staphylococcus aureus isolated from bovine milk. *Zoonoses Public Health* 57, 197–203.

Wellenberg GJ, van der Poel WH, Van Oirschot JT (2002). Viral infections and bovine mastitis: a review. *Veterinary microbiology*.Aug 2;88(1):27-45.

Yen, H.-W., Yang, S.-C., Chen, C.-H., Jesisca, Chang, J.-S., (2015). Supercritical fluid extraction of valuable compounds from microalgal biomass. Bioresour. Technol. 184, 291–296.

Yin, R.L., C. Li, Z.T. Yang, Y.J. Zhang and W.L. Bai *et al*., (2009). Construction and immunogenicity of a DNA vaccine containing clumping factor A of *Staphylococcus aureus* and bovine IL18. Vet. Immunol. Immunopathol., 132: 270-274.