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Capsicum annuum and Capsaicin in Bovine Udder Health: Pharmacological Basis, Experimental Evidence and Prospects for Subclinical Mastitis Management

Farrah Deeba[1]*, Anas Sarwar Qureshi[2], Ghulam Murtaza Awan[3], Muhammad Tayyab[3], Muhammad Adil[1] and Sulaiman Haider[1]

1. Department of Clinical Medicine & Surgery, University of Agriculture, Faisalabad, Pakistan.
2. Department of Basic Sciences, Riphah College of Veterinary Sciences, Riphah International University, Pakistan.
3. Department of Animal & Poultry Production, Faculty of Veterinary & Animal Sciences, Gomal University, Dera Ismail Khan, Pakistan

*Corresponding Author: **farrah.deeba@uaf.edu.pk**

ABSTRACT

Subclinical mastitis (SCM) remains a major constraint on dairy productivity because of its association with intramammary inflammation, increased somatic cell count (SCC) and impaired milk quality without apparent clinical manifestations. Growing concerns regarding antimicrobial resistance have stimulated interest in plant-derived bioactive compounds as potential complementary therapeutic agents. *Capsicum annuum* (red chilli pepper) contains capsaicinoids, particularly capsaicin, which exhibit antimicrobial, antioxidant and immunomodulatory properties. Experimental investigations have demonstrated capsaicin-mediated inhibition of mastitis-associated *Staphylococcus aureus*, including interference with bacterial efflux mechanisms and biofilm formation. Its interaction with the transient receptor potential vanilloid 1 (TRPV1) receptor also provides a pharmacological basis for investigating host inflammatory responses. This review evaluates the phytochemical characteristics, biological mechanisms and experimental evidence supporting the application of *C. annuum* in dairy cattle. Although preliminary findings are encouraging, direct clinical evidence of its efficacy against naturally occurring SCM remains limited. Further investigations are required to establish appropriate formulations, therapeutic dosages and mammary safety.

Keywords: *Capsicum annuum*; Capsaicin; Bovine mastitis; Somatic cell count; Antimicrobial resistance; Oxidative stress

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Introduction

Mastitis is an inflammatory disorder of the mammary gland and remains one of the most economically important diseases in dairy cattle. Its subclinical form is particularly challenging because affected animals generally show no visible abnormalities in udder appearance or milk secretion. Nevertheless, intramammary inflammation increases SCC, interferes with normal milk synthesis and reduces dairy production efficiency [1].

The disease is associated with several bacterial pathogens, particularly *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus uberis* and *Escherichia coli*. Persistent infections caused by *S. aureus* are especially difficult to manage because of bacterial adhesion, intracellular survival, biofilm formation and antimicrobial resistance [1]. Although antimicrobial therapy remains an important component of mastitis management, inappropriate antibiotic administration and repeated exposure to antimicrobial agents contribute to the selection of resistant bacterial populations. Consequently, phytotherapeutic compounds have attracted increasing attention as potential complementary approaches to conventional veterinary treatment. In Pakistan, traditional veterinary medicine provides an important basis for investigating plant-derived mastitis treatments. Dilshad et al. documented 25 medicinal plant species used for mastitis management among traditional veterinary practitioners in Sargodha. *Capsicum annuum* was among the most frequently reported plants, with 32 recorded mentions among 217 traditional veterinary healers [2].

This ethnoveterinary evidence establishes its traditional relevance and provides a rationale for investigating its pharmacological properties using modern experimental approaches.

2. Phytochemical Characteristics and Bioactive Constituents

Capsicum annuum, belonging to the family Solanaceae, contains several biologically active phytochemicals, including capsaicinoids, carotenoids, flavonoids, phenolic compounds and vitamins.

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is the principal pungent compound responsible for the characteristic burning sensation of chilli peppers. Other important capsaicinoids include dihydrocapsaicin and nordihydrocapsaicin. Capsaicin is a lipophilic vanilloid compound with diverse pharmacological activities. Its biological effects are associated with interactions with cellular membranes, sensory receptors and several intracellular signalling pathways [3]. The concentration of capsaicinoids varies considerably according to cultivar, fruit maturity, environmental conditions and extraction procedures. Therefore, crude chilli extract, chilli powder and purified capsaicin should be considered distinct preparations rather than interchangeable therapeutic agents. For veterinary applications, standardization of capsaicin concentration and formulation stability is essential to ensure reproducible biological activity.

3. Antimicrobial Pharmacology: Interference with Bacterial Survival

One of the most important research areas concerning capsaicin is its potential activity against antimicrobial-resistant bacteria.

3.1. Modulation of bacterial efflux mechanisms

Bacterial efflux pumps contribute to antimicrobial resistance by actively transporting antimicrobial substances outside bacterial cells, thereby reducing intracellular drug concentrations.

Kalia et al. demonstrated that capsaicin acts as an inhibitor of the NorA efflux pump in *S. aureus*. Experimental findings indicated that capsaicin enhanced the activity of ciprofloxacin against tested bacterial strains and reduced intracellular invasion of *S. aureus* in macrophages [4].

This mechanism is particularly relevant to mastitis research because intracellular persistence of *S. aureus* may contribute to recurrent and difficult-to-treat intramammary infections.

However, NorA inhibition should not be interpreted as universal reversal of antimicrobial resistance. Its effectiveness depends on the bacterial species, resistance mechanism and antimicrobial agent involved.

3.2. Disruption of bacterial biofilm development

Biofilm formation is an important virulence-associated property of mastitis pathogens. Bacteria within biofilms are embedded in an extracellular matrix that provides protection against environmental stress, antimicrobial exposure and host immune responses.

Mohan et al. investigated the antibiofilm activity of capsaicin and berberine in combination with quinolone antibiotics against *S. aureus* isolated from bovine mastitis.

Their investigation demonstrated improved antibacterial and antibiofilm activity following combination treatment, indicating the potential of capsaicin as an antimicrobial adjunct [5].

These findings provide a mechanistic basis for further investigation of capsaicin-based combination therapies. Nevertheless, laboratory evidence cannot independently establish clinical synergy or therapeutic success in infected cattle.

4. Host-Response Modulation and Oxidative Homeostasis

Mastitis involves a complex interaction between invading microorganisms and the host immune response. During intramammary infection, activated neutrophils produce reactive oxygen species (ROS) to eliminate pathogens. Excessive ROS production, however, can damage mammary epithelial cells, disrupt cellular membranes and aggravate inflammatory tissue injury. Capsaicin and other chilli-derived phytochemicals have demonstrated antioxidant and immunomodulatory properties in experimental models.

4.1. Regulation of inflammatory signalling through TRPV1

Capsaicin primarily interacts with the transient receptor potential vanilloid 1 (TRPV1) receptor, a non-selective cation channel expressed predominantly in sensory neurons.

Activation of TRPV1 increases intracellular calcium concentrations and initiates downstream signalling pathways involved in nociception, neurogenic inflammation and sensory responses [3].

Depending on the concentration, duration of exposure and physiological environment, capsaicin may produce different biological responses. Therefore, it should not be described as an exclusively anti-inflammatory agent. The involvement of TRPV1 in bovine mammary inflammatory regulation remains an important area for future investigation.

4.2. Antioxidant defence and inflammatory biomarkers

Experimental studies involving dietary capsaicin supplementation have provided encouraging evidence regarding its effects on antioxidant defence and immune function in dairy cattle. Li et al. investigated dietary capsaicin supplementation in 20 periparturient Holstein cows. The supplemented group received 1.2 g capsaicin per animal per day from 28 days before calving until 21 days postpartum. The investigators reported reduced milk SCC and pro-inflammatory cytokines, including TNF-α, IL-1β and IL-6, alongside increased antioxidant enzyme activities, including superoxide dismutase, glutathione peroxidase and catalase [6].

These findings support the potential immunomodulatory and antioxidant properties of dietary capsaicin. However, the investigation concerned transition-period supplementation rather than treatment of confirmed intramammary infection. Future mastitis investigations should include total antioxidant capacity (TAC), total oxidant status (TOS), malondialdehyde (MDA), SOD, CAT and GPx to determine whether capsaicin can improve mammary oxidative balance during infection.

5. Implications for Milk Production and Mammary Function

Milk composition is closely associated with the physiological condition of the mammary gland. Intramammary infection may alter milk fat, protein, lactose, minerals and electrical conductivity through epithelial damage and inflammatory changes. SCC and CMT are important screening tools for detecting subclinical inflammation. However, bacteriological culture remains necessary to identify the causative organism and establish bacteriological cure [1]. The nutritional and productive effects of capsaicin supplementation have also been investigated independently of mastitis treatment. Orzuna-Orzuna et al. conducted a meta-analysis involving 13 studies on dietary capsaicin supplementation in dairy cows. Their findings indicated significant improvements in dry matter intake, milk yield, feed efficiency and milk fat concentration. However, capsaicin did not significantly affect milk protein yield, lactose yield or milk SCC [7].

These findings suggest that capsaicin may influence dairy production and metabolic efficiency. Nevertheless, improved milk yield or fat concentration cannot be considered evidence of mastitis recovery.

Similarly, restoration of milk calcium, zinc, copper, density and pH following capsaicin administration has not been adequately established through controlled clinical investigations.

6. Translational Evidence and Research Significance

The available literature provides three complementary lines of evidence: traditional veterinary application, laboratory antimicrobial activity and experimental dietary supplementation.

The distinction between these evidence categories is essential when evaluating the practical therapeutic potential of *C. annuum*.

Table 1. Principal experimental evidence supporting the potential application of *Capsicum annuum* and capsaicin in dairy cattle

References	Research approach	Major findings and significance
Dilshad et al. (2010) [2]	Ethnoveterinary survey in Pakistan	*C. annuum* was among the frequently reported medicinal plants for mastitis management.
Kalia et al. (2012) [4]	Capsaicin against *S. aureus*	Demonstrated NorA efflux-pump inhibition and reduced intracellular bacterial invasion.
Mohan et al. (2022) [5]	Capsaicin and quinolone combination against bovine mastitis *S. aureus*	Demonstrated improved antibacterial and antibiofilm activity under laboratory conditions.
Orzuna-Orzuna et al. (2024) [7]	Meta-analysis of 13 dairy cow studies	Reported improvements in milk yield and fat parameters, without a significant effect on milk SCC or protein yield.
Li et al. (2025) [6]	Dietary supplementation in 20 periparturient cows	Reported reduced SCC and inflammatory cytokines and improved antioxidant enzyme activities.

Collectively, these investigations provide a scientific foundation for further research into capsaicin-based veterinary applications. Nevertheless, none of the cited investigations establishes that purified capsaicin or crude *C. annuum* extract independently produces a confirmed bacteriological cure of naturally occurring SCM in dairy cattle.

7. Research Priorities and Veterinary Application

Despite promising experimental observations, several scientific and pharmacological challenges must be addressed before capsaicin can be incorporated into routine mastitis treatment protocols.

Formulation and dose optimization: Standardized preparations containing defined capsaicinoid concentrations should be developed. Oral dietary supplementation and intramammary administration require separate dose-response investigations.

Mammary tissue safety: The potential irritant effects of concentrated capsaicin must be evaluated before considering intramammary application. Local tissue tolerance, systemic exposure and possible adverse reactions require investigation.

Bacteriological validation: Future clinical trials should evaluate pathogen-specific bacteriological cure rather than relying exclusively on CMT scores or SCC reduction.

Combination antimicrobial strategies: Potential interactions between capsaicin and conventional antibiotics should be investigated through MIC, minimum bactericidal concentration, checkerboard and time-kill assays.

Milk safety assessment: Milk composition, sensory characteristics, possible residues and withdrawal requirements should be evaluated before commercial veterinary application.

Randomized controlled trials involving naturally infected dairy cows should compare standardized capsaicin preparations, conventional antimicrobial treatment, combination treatment and appropriate controls. Clinical outcomes should include bacteriological cure, SCC, milk yield, milk composition, oxidative biomarkers and recurrence rates.

8. Conclusion

Capsicum annuum represents a scientifically interesting source of bioactive compounds, particularly capsaicin, with potential applications in veterinary medicine and bovine udder-health management. Its ability to interfere with bacterial efflux mechanisms, influence biofilm-associated bacterial survival and modulate host antioxidant and immune responses provides a promising pharmacological basis for further investigation.

Evidence from bovine mastitis isolates, dietary supplementation studies and ethnoveterinary investigations supports continued exploration of this plant as a potential complementary therapeutic resource. However, the distinction between experimental antibacterial activity, nutritional supplementation and clinical treatment of intramammary infection must be maintained.

Future research should prioritize standardized formulations, mammary tissue safety, effective dosage determination and controlled clinical trials. Scientifically validated capsaicin-based interventions may eventually complement conventional mastitis management and contribute to responsible antimicrobial use and sustainable dairy production.

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