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Editorial

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New Therapeutic Strategies to Control and Treatment of Bovine Mastitis

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Bovine mastitis, which is an inflammation of the mammary gland frequently resulting from bacterial infection, causes the majority of economic losses to the dairy producers. The prevalence of mastitis in dairy cattle is relatively high. Bovine mastitis can be classified based on clinical futures as clinical or subclinical. Both forms produce significant economic losses due to rejected milk, degraded milk quality, early culling of cows, drug costs, veterinary expenses and increased labour costs for the farmer. Moreover, subclinical mastitis is the main form of mastitis in modern dairy herds, exceeding 20 to 50% of cows in given herds. The cost of subclinical mastitis is very difficult to quantify, but most of the researchers agree that it can be up to 40 times more common than clinical mastitis. In India, the estimated loss due to mastitis is around Rs. 16,702 million per annum. Subclinical mastitis was found more important in India than clinical mastitis especially in cows (10-50%) and buffaloes (5-20%). The predominant causal organisms of mastitis are cell-walled bacteria, although mycoplasma, yeast and algae have also been reported to cause mastitis. Various predisposing factors like physiological, genetic, pathological or environmental may contribute to the emergence of mastitis in dairy cattle. Presently antibiotics are used for the treatment of mastitis. However, therapeutic success rate is poor due to indiscriminate use of antibiotics leading to development of multiple drug resistant pathogens. Besides this, major problems in bovine mastitis with intracellular pathogens like *S.aureus* because of poor cure rate. These facts highlight the need for completely newer strategies for treatment of mastitis.

PERSPECTIVES FOR NEW THERAPEUTIC STRATEGIES

Nanotechnology

Wide range of antibiotics have been used for the past 40 years in the control of bovine mastitis. However, because of the emerging antibiotic resistance mainly due to their overuse and other possible mechanisms for poor cure rate in mastitis include: (i) low intracellular uptake of commonly-used drugs, (ii) the non-diffusion of acidic antibiotics at neutral extracellular or cytoplasmic pH through the lysosomal membrane, (iii) the very poor retention in cells. For all these reasons, activity is not expected to be very long-lasting when antibiotics are administered as aqueous solutions. Thus, there is definitely a need for more specialised dosage forms to be developed for use in the treatment of *S. aureus* bovine mastitis. Nanotechnology has enabled researchers to synthesize nanosized particles (less than 100 nm), using them in a wide range of applications, particularly in drug delivery. Nanoparticles possess increased surface areas and therefore have increased interactions with biological targets (such as bacteria) compared with traditional, micronparticles. Moreover, nanoparticles are much more likely to enter cells than micron particles. As a whole, nano-antibacterial particles will posses stronger effects on bacteria than their micro-counterparts. The nanoparticles may be considered potential delivery systems in the treatment of bovine mastitis since they may be taken up by the phagocytes. Moreover, the literatures indicate that it is possible to incorporate antibiotics in most of the nanoparticles delivery system. The main challenge appears to be to obtain a high antibiotic loading within these delivery systems.

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Mastitis Vaccines

Mastitis vaccines have been formulated with the hope of reducing the incidence mastitis in dairy farming and promoting the profit of industry. The use of killed whole cell vaccines to manage infectious diseases on-farm in dairy cattle is common, and vaccination against mastitis pathogens is no exception. Many researches have been made to develop a vaccine against mastitis, but few have claimed satisfactory outcomes. It is clear that a single vaccine will not prevent mastitis caused by the plethora of pathogens and their different mechanisms of pathogenesis. All vaccinations should be done according to manufacturer recommendations. Vaccinating both cows and heifers for coliform and *S.aureus* has been shown to be worthwhile in different study. Coliform vaccines can reduce the incidence, severity and duration of infections in both lactating cows and heifers. *S.aureus* vaccines can reduce the incidence of new intra-mammary infection as well as increase the spontaneous cure rate, and should be used in herds in which this type of organism is a major problem.

Bacteriophage Therapy for Mastitis

One of the alternative treatments for mastitis is bacteriophage therapy, which uses pathogen specific bacteriophages in the treatment of a bacterial infection. Some studies indicate that phage therapy could produce beneficial effect against *E.coli* and *S.aureus* induced mastitis infection. However, additional further research is required to explore the therapeutic potential of bacteriophages to treat clinical and subclinical mastitis associated bacterial infections.

Cytokines

The roles of the various immune system components in mammary gland defence against infection are not well understood. However, cytokine production and leukocyte populations play important roles in host defence and pathophysiological processes during bacterial infection. Several cytokines have been identified as major actors during the acute-phase reaction (complement component, interleukins (IL)-1, -2, -6 and -8 and tumour necrosis factor alpha). They possess chemotactic activity responsible for leukocyte recruitment and activation and they can also enhance bactericidal activity of phagocytes. Many experimental studies indicate that infusion of cytokines with or without antibiotics increased the cure rate in *S. aureus* infected mastitis. Finally, cytokines therapy seems to be a promising approach but further studies have to be done to confirm therapeutic interest.

Recombinant Mucolytic Protein

Nowadays recombinant protein technology plays an important role in animal disease control. An alternative to the use of antibiotics for *S. aureus* mastitis may be the use of a recombinant mucolytic protein such as lysostaphin. The potential value of an intramammary administration of lysostaphin was assessed in experimentally-induced *S. aureus* mastitis. However, the authors suggested that an improved formulation of recombinant lysostaphin may prove to be an effective alternative to antibiotic therapy for bovine mastitis. The advantage is that it can potentially circumvent the problems associated with current antibiotic therapy because of its targeted specificity, because it offers low toxicity and due to the possible benefits of not having to discard milk containing biologically-active residues.

CONCLUSIONS

Mastitis remains a major challenge to the worldwide dairy industries, but still there is no established treatment for such problem. Currently, the use of antibiotics is the most common method of treatment of bovine mastitis. Nevertheless, this type of method has some demerits due to low cure rate, increasing occurrence of resistance and the presence of antibiotics residues in the milk. Therefore, an alternative to antibiotics was investigated by several researchers in order to find an effective approach for management of bovine mastitis. Nanoparticles, Vaccines, Bacteriophages and cytokines are some examples of valid substitutes to antibiotics to control bovine mastitis.