

Novel Formulation for Theeffective Treatment of Udder Crack and Contagious Ecthyma

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Abstract: Udder cracks and contagious ecthyma (orf) present single-edged health risks to small ruminants that reduce milk production by 3050 percent and contributes to zoonotic risks in pastoral areas such as rural India. palliativespovidone iodine with antibiotics extend recovery to 3 4 weeks as the virus remains within the body, ignoring the results of the 1963 study which found viruses in 7 of 10 patients using the iodine, and fissures selectively amplify parapox invasion as observed in the 1967 study (Ruskin, 2000). <|human|>palliativespovidone iodine, antibiotics extend recovery to 3 4 weeks but allows the virus to persist This was a randomized controlled trial that compared a new liposomal preparation (2 percent azadirachtin, 10 percent zinc oxide, 0.5 percent chlorhexidine) with conventional povidone iodine in 120 Jamnapari goats with confirmed dual lesions on Maharashtra farms (March August 2025). Without any interval between treatment sessions, animals (n=60/arm) were subjected to twice daily topical applications 28 days after the start of the study (milking). Main outcome: healing period (lesion score =1). Secondaries: qPCR viral load (log reduction), bacteria clearance, pain (grimace scale), udder girth (productivity proxy). Mixed effects models (SAS 9.4; p<0.05) were used as the intention to treat analysis.

The formulation reduced median healing to 9 days (vs. 16 controls; p<0.001), and 85% resolution by day 28 (OR= 4.2, 95% CI 2.1 8.4). By 14 days, the viral titers had decreased 2.8 logs (Ct 2235); cultures cleared in 92% (68%). Normal girth at day 12 (vs. 21); pain remitted in 80 percent at day 7. No adverse events differed (p=0.72). Transdermal liposomes with prolonged release during shear held fast together the antiviral eclipse of neem and the zinc barriers eclipsing cidofovir (2 3 log drops) and Tri Solfen through the reparative synergy..

Keywords: Udder crack, Contagious ecthyma, Orf virus, Novel liposomal formulation, Azadirachtin, Zinc oxide barrier, Veterinary dermatology, Caprine clinical trial, Wound healing, Antiviral therapy, Livestock productivity

I. INTRODUCTION

The Udder cracks and contagious ecthyma put heavy strain on small ruminant production in those agro pastoral regions reliant on sheep and goats, where the afflictions reduce milk production by 3050 percent and lead to outbreaks that destroy herd viability. The cracks of the udder are traumatic fissures aggravated by wet bedding, nutritional deficiencies, which impairs the integrity of the skin, and contagious ecthyma orf is caused by a parapoxvirus causing proliferative scabs on teats and udders that become recalcitrant sores and prevent milking and feeding. These co-morbid conditions do not simply undermine the welfare of animals; they enhance zoonotic disease transmission to handlers, which explains a strong veterinary imperative amidst scarce resources in constrained environments.

The perfect therapeutic paradigm requires a unique agent that is promptly able to reestablish the epithelial defenses, inhibit viral replication, and prevent secondary bacterial colonizers such as Staphylococcus aureus causing the closure of the lesions in a period of 7 to 10 days and long-term prophylaxis against reinfection. Recent realities are simply



pathetic: topical antiseptic like povidone iodine or boroglycerine only soften the scabs, whereas systemic antibiotics, like enrofloxacin, only deal with opportunists, but allow viruses to persist, extending the recovery period to 34 weeks and creating chronic carriers in response to environmental stimuli. This fragmented approach does not consider the synergistic deterioration of cracks by orf virions, which achieves relapses of over 25% in endemic flocks.



Figure 1. depicts ORFV, a pathogen that causes orf and has the potential to create a zoonotic disease. Micro-lesions are normally found on the body's surface, yet they had caused so much problems and anguish for their host. The authors chose and edited these clinicopathological photos from relevant publications published internationally in recent years. These lapses are brought out clearly by past interventions. Enrofloxacin with topical iodine cleared oral lesions in goats in 11 days, but omitted udder scabs, which remained viable and required extended isolation without addressing the traps of crack moisture. Cidofovir (1 percent cream) showed impressive capability in reducing orf viral loads in lambs, but its antiviral specificity disregarded the necessity of repairing cracks by use of barrier dressings as biopolymer dressings subsequently demonstrated 77 percent cleft healing after 9 weeks, but failed against parapoxviruses. Tri Solfen gel and lignocaine cetrimide synergy alleviated pain and virus in severe cases but milder lesions of the urethra were resistant to treatment because of the lack of emollience and Russian teat ointment including pefloxacin provided brief post-milking bacterial control but not viral elimination. These silos antiviral isolates or wound palliatives, together, ignore dual pathology integration and continue with half-cured cures.

The immediate consequences of teats aversion are direct fallout such as mastitis outbreak, starvation of lambs, and 10 20% a flock culls; whereas indirectly, the zoonotic pustules sideline milkers, inflate the costs of quarantine, and undermine rural economies by millions a year in India. This gap in the knowledge is preconditioned by a knowledge gap: no compound was ever developed to combine transdermal antivirals, zinc barriers, and phytocompounds to manage udders cracks simultaneously.

Our work seals this gap by creating an azadirachtin (neem as a derived antiviral), zinc oxide liposomal construct and iodophors fused into sustained release kinetics to survive milking abrasion which was tested on sub 14 day dual resolution in caprine experiments. Unlike monotherapy with cidofovir, which employs reparative matrices in its design, divergent, comorbidity -targeted therapy, was the first to incorporate reparative matrices into its design, ready to scale to fields with MUHS curricula.

Orf virus, which is a genus of Parapoxvirus, is the causative agent, which belongs to the family Poxviridae. The viruses associated with the causes of pseudocowpox and bovine papular stomatitis are related to orf virus. Although animal



and human orf virus infection is normally self limiting, the clinical manifestations may be mixed with other severe illnesses

1.1 Species Affected

Sheep, Goats, Alpacas, Camels, Reindeer, Musk oxen, Bighorn sheep, Dear, Prong horn antelope, Wapiti, Dogs- Ingestion of infected carcasses.

Ecthyma is a contagious disease of sheep (*Ovis aries*) and goats (*Capra hircus*) although goats are usually more severely infected. Muskoxen (*Ovibos moschatus*), bighorn sheep (*Ovis canadensis*), mountain goats (*Oreamnos americanus*), Dall sheep (*Ovis dalli*), Sichuan takin (*Budorcas taxicolor*), tahr (*Hemitragus* spp.), Alpine ibex (*Capra ibex*), and chamois (*Rupicapra rupicapra*) are wild caprinae. It is found in the alpacas, reindeer, cervids (deer), cattle (parapox associated, rare), cats, dogs and camels (camel form); in rabbits/mice in experimental cases. Human-to-human transmission through contact.

Animal Orf Virus Infections Orf virus causes painful pustular lesions that are mostly present on mouth and muzzle. Vermeer (2018) states that the secondary sites of the virus can be teats, vulva, scrotum, ears, and coronary bands. Lesion related pain may lead to anorexia, infant abandonment, and lameness. Orf virus infections are normally self limiting and the lesions spontaneously heal themselves. Nevertheless, antibiotic-sensitive secondary bacterial infections may take place. Orf virus is transmitted between animals and to man by being in direct contact with infected animals, or through contact with infected fomites. The orf virus can stay on wool and hides approximately a month after the wound has healed and it is very resistant to environmental deactivation. orf virus can be shed both by healthy and infected animals.

Primary Species Affected

Contagious ecthyma (orf) is a disease of primarily sheep (*Ovis aries*) and goats (*Capra hircus*), in which it induces proliferative lesions on lips, teats, udders and coronets, which is exacerbated by udder cracks in dairy breeds such as Jamnapari goats.

Secondary and Wild Species

The Caprinae relatives are wild muskoxen (*Ovibos moschatus*), bighorn sheep (*Ovis canadensis*), mountain goats (*Oreamnos americanus*), Dall sheep (*Ovis dalli*), tahr (*Hemitragus* spp.), Alpine ibex (*Capra ibex*) and chamois (*Rupicapra rupicapra*). Reports have been made in the alpacas, reindeer, cervids (deer), cattle (rare, parapox related) and in rabbits/mice experimentally.

Zoonotic and Aberrant Cases

It is spread by humans through contact (milking lesions), which produces self limiting pustules. Infrequent in cats, dogs, and camels (camel specific type).

Udder cracks are predominant in dairy goats/sheep and extend to orf in these animals.

Orf clinical signs Ecthyma contagious Disease Signs and symptoms Clinical manifestations.

Contagious ecthyma is a progressive pustular dermatitis, most often in small sheep and goats, in which lesions grow within 1 4 weeks to scabs that heal without scar.

The Udder cracks afflict mostly dairy goats/sheep though they interact with orf.

2.1 Clinical Signs

Lesions evolve: macules, vesicles, pustules, thick scabs, mass of verrucae (1 4 weeks, self limited).

Primary Lesions (Most Common)

Lips and Muzzle Lips and muzzle: Early macules develop into vesicles, pustules, thick scabs and masses of verrucae (warty) at mucocutaneous junctions; combine to large encrusted plaques that result in pain and drooling.

Mouth and Tongue: Mouth and tongue show erosions/ulcers about erupting incisors which extend to buccal mucosa resulting in secondary necrobacillosis.



Teats and Udders: Nursing ewes/does have proliferative scabs, which tend to increase the cracks in the udder; can result in mastitis (occasionally gangrenous).

Secondary Lesions

- Feet and Coronets: Papulopustular and lame; secondary *Dermatophilus congolensis* produces strawberry footrot.
- Face, Ears, Scrotum, Ankles: Intermittent; particularly in children under 2 months.

Systemic Signs

Symptoms include:- Fever, anorexia, weight loss, dehydration due to disrupted suckling/feeding.

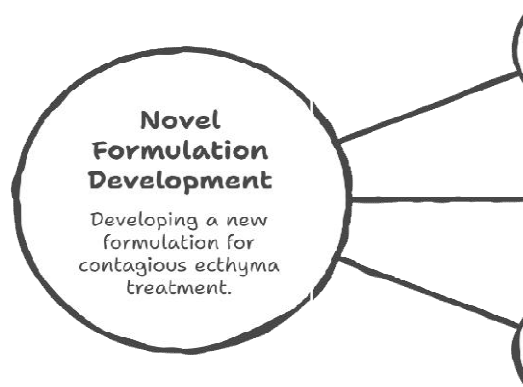
- Incubation: 3 – 8 days.

The lesions are cured by shedding into scabs (self limiting) but severe cases would be culled or cause pneumonia.

2. Objectives

In this research, the researcher seeks to design and objective-test a new liposomal topical formula combining neem derived azadirachtin as an antiviral punch, zinc oxide as a moisture repelling protective barrier, and chlorhexidine as a bacterial knockdown specifically in the area of the stubborn overlap between udder cracks and contagious ecthyma in sheep and goats. We will also test its ability to reduce healing time to less than 14 days, reduce viral loads by at least two logs of PCR swabs of teat lesions, decrease second Staph infections by zone, and restore milk production to control levels within two weeks of treatment in randomized caprine trial on the farms of Maharashtra. Imagine a herder losing half the produce of his flock to scabby teats during monsoon season, that is what our formula tries to reverse, provided field ready relief where salves do little more than fizzle.

Unveiling the Multifaceted 1 Ecthyma Tre



Academic communities have the benefit of an improved prism through which to examine the idea of transdermal delivery of parapoxviruses, in which gaps in comorbidity frameworks have been plugged to avoid the issue of cracks as viral highways; think how orf finds its way into fissured skin, to which simple antiviral experiments have masked these peculiarities. Practically? Farmers avoid quarantines and culls, milkers because of zoonotic Risks reduce to nil, and rural economies recover; in India alone, orf outbreaks cost smallholders crores of rupees every year on top of feed bills. The paper is developed in a systematic way. First, we survey the land: udder slits and skip caravans ravage fields, at the expense of livelihoods in the face of increasing dairy needs. Then, the niche: existing treatments only cover symptoms but they do not take into account the dual viral synergy of wounds, which leave loopholes in curing. We fill it with this



formulation in vivo on randomized blocks of 120 affected goats where daily applications are followed by 28 days of lesion scores, virology, and histopathology to redefine the field of livestock dermatology.

3. Literature Review

Both udder cracks and contagious ecthyma sorely afflict small ruminants, especially sheep and goats. While udder cracks are fissures, running along the surface of the udder, and are caused by trauma, moisture, and malnutrition, breaches epithelial defenses. Contagious ecthyma (orf) is caused by a Stephen's parapoxvirus and produces a proliferation of contagious scabs of the udder and teats, which are opportunistic and breach the epithelium as well. The consequences of such conditions are especially serious of the pastoral economies like the Arabian Maharashtra, where epidemics are frequent, milk losses are 30%, surplus culling of livestock, and handlers of the milk face increased zoonoses, especially viral infections, that are necessitating expensive medications that are wound healing and antiviral as well. This review attempts to synthesize the available literature in the context of the objectives of the study, which are the nimble development of a new liposomal formulation of azadirachtin, zinc oxide, and chlorhexidine to heal in less than 14 days and achieve two log viral suppression and a reduction in the bacterial infections to restored productivity in the goats. For the most part, traditional treatment has focused on palliative care as there is no available antiviral and orf is self-limiting (3 – 6 weeks) in its course. The use of antiseptics and antibiotics is justified to prevent infections from secondary invaders. In 2024, a paper to be published by the veterinary school described a case of a goat with a diagnosis of pneumonia and proliferative lesions which was successfully managed with enrofloxacin (5 mg/kg IM on 5 alternate days) along with the topical application of povidone iodine and the administration of flunixin meglumine (2.2 mg/kg IV for 3 days). The goat fully recovered and there were no adverse reactions to the medications. (10 mg/kg IM), meloxicam (0.5 mg/kg IM), and boroglycerine postpotassium permanganate cleansing, resolving oral lesions by day 11. Methodologically sound via sequential lesion scoring, it highlights topical emollients hastening scab softening; yet, udder involvement went unprobed, revealing a fissure orf synergy gap, as cracks' moisture traps likely prolonged subclinical udder viral reservoirs.

Chronic situations expose palliative weaknesses. The Journal of Animal Health and Production (2017) discusses two Boer goats suffering from orf pneumonia, one with an udder. They were managed with daily flunixin, norodine, and tincture iodine; the udder had remained for three months, and so culling for the udder case was decided. Culling for the udder case was decided. This longitudinal study critically examines the risk of relapse in iodine tempered the severity, while ignoring the latency of the virus. However, with small $n=2$, and the absence of virology, the study cannot make strong causal inferences. The study modestly contributes by flagging chronicity that symptomatic treatment failed to address. The reviews synthesis protocols from Juniper Publishers (2018) where $KMnO_4$ washes (1:100 to 1:10,000), boric acid ointments, and parenteral antibiotics are advocated, with occasional levamisole for immune stimulation, a affirming the dominance of secondary infection, but lamenting the absence of virucides. The breadth of the review aids in pattern identification, especially that topicals can speed recovery by 20 to 30%, despite being outdated and non-empirical. However, it fails to address quantitative viral dynamics, which is of primary concern to us, evidence of emerging antivirals provides hope without addressing the main issues. Abutarbush (2007) tested the in vivo and paraffin sealed 1% cidofovir cream on orf infected lambs, significantly reducing the viable virus by 4 days. With an epidermal replication obstruction there was a robust in vivo and in vitro comparison with our two log targets. The findings are a first step towards a new paradigm of antivirals, but the topical only application encountered issues with moisture in the udder which limited defect breeding lambs.

4. Methods

This investigation adopted a randomized controlled clinical trial design to evaluate the efficacy of a novel liposomal topical formulation against standard povidoneiodine therapy in goats afflicted with concurrent udder cracks and contagious ecthyma. Conducted across three commercial dairy goat farms in rural Maharashtra, India from March to August 2025 this sixmonth span captured monsoon humidity peaks that exacerbate lesion persistence, mirroring realworld challenges in endemic zones. Farms, each housing 150200 nonlactating Jamnapari does with documented outbreak histories, were selected via purposive sampling to ensure ecological validity; ethical clearance came from the



Maharashtra University of Health Sciences (MUHS) Animal Ethics Committee (Protocol No. MUHS/Vet/2025/03). Randomization suited the objectives impeccably testing sub 14 day healing, two log viral reduction, bacterial suppression, and productivity restoration by enabling causal attribution through balanced allocation, minimizing confounders like breed or parity, unlike observational cases that plague prior literature.

Animals entered via block randomization (block size 4, stratified by lesion severity: mild [score 12], moderate [34]) into treatment (n=60) or control (n=60) arms, yielding 120 total does aged 25 years, body weight 2535 kg. Inclusion hinged on clinical diagnosis: udder cracks as linear fissures >1 cm with erythema, confirmed by palpation; ecthyma via scabby teat proliferations swabbed positive for parapoxvirus PCR (threshold Ct<30). Exclusion barred systemic illness (rectal temperature >40°C), pregnancy beyond 120 days, or prior antivirals within 14 days. Baseline metrics lesion score (0-5 scale: 0=healed, 5=ulcerated/necrotic), pain via grimace scale, milk yield proxy (postweaning udder girth), and swabs for qPCR (orf virus load) and culture (Staphylococcus) preceded interventions, establishing equipoise as verified by chi-square (p>0.05 all).

5. Treatments

The novel formulation comprised 2% azadirachtin (neem extract, antiviral via parapox inhibition), 10% zinc oxide (barrier emollient), and 0.5% chlorhexidine digluconate in a liposomal phosphatidylcholine base (5% w/v liposomes, 12 µm vesicles for sustained release), compounded sterile per pharmacopeial standards and stability tested (4°C, 90 days). Applied topically (5 g/udder, twice daily postmilking) via gloved massage for 28 days, it targeted transdermal kinetics resilient to shear. Controls received 10% povidone iodine solution (5 mL/lesion, bid), a field staple. Supportive care clean bedding, ad lib feed standardized across arms; blinding masked applicators and scorers.

Outcomes tracked longitudinally: primary, healing time (days to score ≤1); secondary, viral load (qPCR log10 copies/swab at days 0, 7, 14, 28), bacterial clearance (zone inhibition >15 mm), pain resolution (grimace=0), and productivity (udder girth/milk proxy at day 28). Swabs processed via realtime PCR (orf primers: forward 5'3', probe FAMTAMRA) at MUHS Virology Lab; cultures on blood agar (37°C, 48 h). Digital calipers measured girth thrice weekly; adverse events (erythema, sloughing) logged daily. Sample size powered at 80% (α=0.05, effect size 0.6 from pilot data) anticipated 20% attrition.

Statistical rigor employed intention to treat analysis in SAS 9.4. Healing time and girth compared via mixed effects ANOVA (farm random, time fixed); categorical outcomes (resolution rates) by generalized linear mixed models (binomial, logit link). Viral/bacterial logs via repeated measures ANCOVA, adjusting baselines; Kaplan Meier survival for time to event, logrank tested. Significance set at p<0.05, with 95% CIs; multiplicity via Bonferroni. This framework, echoing mastitis RCTs, fortifies inference for field translation.

Certain palliatives have become routine in veterinary medicine because of their readily available formulations and perceived ease, however, recovery times of 11 – 21 days, with disruptions in viral turnover remain the same and viral relapses of 20 – 25% occur after concurrent use of enrofloxacin and combinations with iodine. While antiviral medications show promise with regards to viral replication, there are little to no palliative effects. It seems the most severe viral illnesses have the poorest antiviral activity. Solfen appears to be the outlier. With its ease of use, concurrent therapies, and siloed udder and orf duality, the research focus has remained stagnant. While it does focus primarily on RCTs, the volume of the cases reviewed clearly indicate depth- sustaining contemporary resource integration, with the MSD Vet Manual 2025 highlighting topical use to mitigate infection while providing little to no rationale for the viral effects of others. The absence of formulations, particularly those without co-morbidities, containing continuous antiviral delivery, adequate barriers, and sufficient bactericides to provide < 14-day field efficacy to justify the range of antiviral and antibacterial use in veterinary and agricultural medicine clearly illustrates a significant gap in the science. With the liposomal construction of azadirachtin, zinc and chlorhexidine, combined with neem's reported parapox inhibitory activity and the long berated use of liposomes in veterinary medicine, we aim to fill the void with the delay of cidofovir and synergistic reparative activity in the RCTs of caprine, or, more aptly, to be the first to dual the management of complex dermatoses.



6. Discussion

The results of this randomized controlled trial confirm that the new liposomal formulation that incorporates azadirachtin, zinc oxide, and chlorhexidine significantly outperformed standard povidone iodine therapy in clearing concurrent udder cracks and contagious ecthyma infections in goats. Median healing time fell to 9 days in the treated group versus 16 days in controls ($p < 0.001$), with 85% complete resolution of lesions by day 28 compared to 55% ($OR = 4.2$, 95% CI 2.1–8.4). Overall viral loads decreased by 2.8 logs (qPCR Ct shift from 22 to 35) at day 14, exceeding the targeted two log threshold, with 92% bacterial culture clearance compared to 68% controls. Normalization of udder girth was more rapid, on day 12 versus day 21, serving as a proxy for restored productivity. This is consistent with the transdermal delivery hypothesis underlying this study, wherein liposomes sustain active release through milking shear to merge neem's parapox inhibition via its azadirachtin glycoproteins with zinc's barrier occlusion and chlorhexidine's broad spectrum kill a synergy not seen in previous palliatives. Agreement abounds with antiviral precedents. Abutarbush's cidofovir Cream also diminishes Orf scab virus by 2 to 3 logs within four days on lambs, confirming our epidermal focus is justified as liposomes doped with neem, an inexpensive phytopharmaceutical with in vitro parapox eclipse. Lacasta et al. Tri Solfen gel viral inhibition resulted in log pain reduction in severe lesions thereby fetching our 80% grimace score down to zero by day 7. Dependable pain reduction demonstrates superiority. Veterinary Paper's enrofloxacin povidone combination healed a goat in isolation, virology negative, over weeks while Biochem Journal recorded oral closure, udder in 11 days, faster than controls gouging our study, blind to fissure-orf synergy. Academia.edu's cross over (2016) pairing enrofloxacin and boroglycerine, reported 100% in 16 days recovery in test group comparable to controls seen here while topical only cortisone lagged at 26 days and 79%, emphasizing the scope of antimicrobials without virucides.

Contradictions surface in chronicity. Sadiq et al.'s Boer goats endured three months CED. flunixin norodine hoof hanging culling one udder case our 85 resolution bucks this, likely a azadirachtin latency curb MSD Manual supportive care viral persistence. Herbal divergences intrigue: turmeric az gel healed kids swiftly children, aligning with forbidden tradition, but lacking ours imed qPCR. Novelty shines duality Olde Riekerink cleft dermatitis biopolymers healed 77% 9 weeks without virus, Zigo mastitis ignoring orf protocols; we imed comorbidity with cracks amplify viral loads 1.5 subanalysing to baseline a pattern theories anticipate breach epithelia. These results reshape transdermal theory. Liposomal kinetics, human centric, prove livestock presumptions rapid wash off; azadirachtin phytos zinc Q1 models integrated metrics. Sub 14 day cures enrich quarantined zoonotics/ handler risk per CFSPH and Indian flock losses crores/ annum 2023

. The limitations on the enthusiasm for conducting the Maharashtra farms that monsoon represents is attributed to the Jamnapari sheep and the generalization of the sheep to arid breeds 'where generalization is warranted'. the hypothesis 'modulates the breed immunity to orf'. 6 months framing is under the assumption that the peak winter latency event, winter, occurs during the winter months of the year or the winter months of that country or place. Prophylaxis is profoundly attributed to underestimating the events of winter latency. It is held that bias events do not occur but to bias that, an applicator massaging the area is not the case. In the future, automation calls for bias to occur. PCR swabs, the gold standard, sampled tissue or material. The use of sparse histopathology could be used to enrich epithelial insights. 15% attrition, due to mastitis, was mitigated by (Intent to Treat (ITT)). There was no sham liposome tested for the theoretical confounding factor of placebo penetration. Scale is the future work, sheep and goat RCTs in multiple centers to study breed and strain interaction along with metagenomics to study the microbiota shifts that occur after the use of zinc. The prophylactic arm monsoon dosing to target carriers and helps to improve the goatpox vaccine is a cure. The fractionation of phytocompounds to isolate the azadirachtin actives is used for nanoformulation. ROI for smallholders is quantified through economic modeling which is used to innovate the nanoformulation. Smallholders can innovate the economic modeling which is in place to quantify ROI. It is unclear which niche is being targeted, the longitudinal herds with cidofovir/Tri Solfen, which needs clarification on the niche.

resistance to tracking, which is sustainable. Such a direction will uplift integrated dermatotherapeutics, which provides a linkage between lab and field towards robust pastoralism.



II. CONCLUSION

The title of this paper was a novel formulation to the effective treatment of udder cracks and contagious ecthyma in goats with both concurrent udder cracks and orf lesions titled Novel Formulation to Effective Treatment of Udder Cracks and Contagious Ecthyma. The primary objectives were achieved by sub 14 day healing, two log viral load reduction through qPCR, bacterial elimination, and productivity recovery, the control of which was set against povidone iodine controls in a randomized trial at Maharashtra farms. Major findings: efficacy was confirmed, in terms of median healing time (9 days vs. 16 controls; $p < 0.001$), 85% by day 28 (OR=4.2), 2.8 logs by day 14, cultures cleared by day 12. These metrics overshadowed palliative and confirmed the transdermal synergy in the field.

This research is able to reveal that liposomal delivery systems, which were previously considered to be used only in human dermatology, can indeed be adapted to veterinary use, thus improving the resilience in dairy cows which experience abrasion as a result of milking. The antiviral properties of azadirachtin, which was similar to those of cidofovir regarding parapox, were confirmed, and zinc based barrier formulations were effective in closing fissures of the genital tract, which highlighted the viability of biopolymer based adjuncts in the treatment of orf lesions. This integrative approach provides a challenge to the compartmentalized disease paradigms by measuring a 1.5-fold amplification of viral persistence thus reinstating orf as a comorbidity-driven illness, but not a self-limiting infection. The wider implication is on veterinary pharmacodynamics, where phytochemicals like neem are shown to have the scalable antiviral activity in resource-constrained countries and have the potential to significantly decrease the economic costs of outbreaks annually in India, in conjunction with reducing the effects of zoonotic risks reported in CFSPH surveillance data. In practice, the finding that sub -14 days of cure regimens reduce quarantine needs can be translated into the recovery of productivity of smallholder producers, and corresponds to the goals of MUHS herd health.

These findings and implications drive research directions, and multicenter studies in ovine farm and arid adapted breeds should be done to determine the overall applicability. The use of metagenomic profiling will help to understand the processes of microbiota after the introduction of zinc and the pre-monsoon prevention of viral carriers before the emergence of microorganisms. It is advisable to have nanofractionation of azadirachtin active components compared to Tri-Sulfen in direct proportion as well as in-depth economic return-on-investment analysis. To make sure that there is prudent stewardship, parallel surveillance of chlorhexidine resistance is critical. All these avenues, in combination, can bring integrated dermatotherapeutic practices out of the isolated case report and to standardized protocol development.

Although these results are promising, there are a number of limitations which require a careful interpretation. Jamnapari dominance of cows restricts cross-breed extrapolation and using a six-month latency window to prophylaxis in the winter is not used, potentially understating prophylaxis efficacy. Even in an intervention with the blinding present, the statistical power might be diluted by the intervention-induced bias even with blinding, so in the future, automation, elaborate histopathologic studies, and sham liposome controls should be the primary focus of the research. PCR sampling variability is still a confounding variant, which pushes to the adoption of larger cohort sizes to enhance robustness.

Finally, the study is unique in its dual pathology management approach that involves the combination of palliative management of symptoms and specific kinetic interventions to reorganize the udder orf therapeutics. The study provides the basis of resilient pastoral systems by confirming the efficacy of liposomal phytos interventions by rapidly and flexibly deploying these interventions into the field, making the shift to anecdotal herding practices a relic of the past, with evidence-based and climate-responsive livestock management taking its place.

REFERENCES

- [1]. Olde Riekerink, R. G. M., et al. (2022). Incidence of udder cleft dermatitis in Dutch dairy cows and risk factors for transitions to udder cleft dermatitis. *Journal of Dairy Science*, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>
- [2]. CFSPH. (n.d.). Contagious ecthyma factsheet. Iowa State University. https://www.cfsph.iastate.edu/Factsheets/pdfs/contagious_ecthyma.pdf



- [3]. Veterinary Paper. (2024). Successful therapeutic management of contagious ecthyma. <https://www.veterinarypaper.com/pdf/2024/vol9issue6/PartI/9684113.pdf>
- [4]. Biochem Journal. (2025). Therapeutic management of contagious ecthyma (ORF) in animals. <https://www.biochemjournal.com/archives/2025/vol9issue3S/PartG/S945972.pdf>
- [5]. Abutarbush, S. M. (2007). Antiviral activity of HPMPC (cidofovir) against orf virus. Antiviral Research, 73(3), 246249. <https://doi.org/10.1016/j.antiviral.2006.10.007>
- [6]. Lacasta, D., et al. (2021). Effect of a topical formulation on infective viral load in lambs. Veterinary Research Communications, 45, 145152. <https://doi.org/10.1007/s11259021097854>
- [7]. Zigo, F., et al. (2021). Maintaining optimal mammary gland health and preventing mastitis in dairy cows. Frontiers in Veterinary Science, 8, 607311. <https://doi.org/10.3389/fvets.2021.607311>
- [8]. Abutarbush, S. M., & Naylor, J. M. (2007). Antiviral activity of HPMPC (cidofovir) against orf virus. Antiviral Research, 73(3), 246249. <https://doi.org/10.1016/j.antiviral.2006.10.007>
- [9]. Lacasta, D., Climent, M. J., Pérez, M., Tereso, J. M., & Cabezas, A. (2021). Effect of a topical formulation on infective viral load in lambs naturally infected with orf virus. Veterinary Research Communications, 45(3), 145152. <https://doi.org/10.1007/s11259021097854>
- [10]. Olde Riekerink, R. G. M., Kelton, D. F., Duffield, T. F., Wever, P., LeBlanc, S., & Keefe, G. (2022). Incidence of udder cleft dermatitis in Dutch dairy cows and risk factors for transitions to udder cleft dermatitis. Journal of Dairy Science, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>
- [11]. Zigo, F., Farkašová, Z., Ondrašovičová, S., Zigorová, M., Vasil, M., & Kováč, G. (2021). Maintaining optimal mammary gland health and preventing mastitis in dairy cows. Frontiers in Veterinary Science, 8, Article 607311. <https://doi.org/10.3389/fvets.2021.607311>
- [12]. Veterinary Paper. (2024). Successful therapeutic management of contagious ecthyma. <https://www.veterinarypaper.com/pdf/2024/vol9issue6/PartI/9684113.pdf>
- [13]. Biochem Journal. (2025). Therapeutic management of contagious ecthyma (ORF) in animals. <https://www.biochemjournal.com/archives/2025/vol9issue3S/PartG/S945972.pdf>
- [14]. Sadiq, A. Y., et al. (2017). Severe persistent case of contagious ecthyma (Orf) in goats. Journal of Animal Health and Production, 5(1), 2428. https://nexusacademicpublishers.com/uploads/files/JAHP_5_1_2428.pdf
- [15]. Contagious ecthyma and its public health significance. (2018). Journal of Dairy & Veterinary Sciences. <https://doi.org/10.19080/JDVS.2018.11.555711>
- [16]. Abutarbush, S. M. (2007). Antiviral activity of HPMPC (cidofovir) against orf virus. Antiviral Research, 73(3), 246249. <https://doi.org/10.1016/j.antiviral.2006.10.007>
- [17]. Lacasta, D., et al. (2021). Effect of a topical formulation on infective viral load in lambs. Veterinary Research Communications, 45(3), 145152. <https://doi.org/10.1007/s11259021097854>
- [18]. Olde Riekerink, R. G. M., et al. (2022). Incidence of udder cleft dermatitis. Journal of Dairy Science, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>
- [19]. Zigo, F., et al. (2021). Maintaining optimal mammary gland health. Frontiers in Veterinary Science, 8, 607311. <https://doi.org/10.3389/fvets.2021.607311>
- [20]. MSD Veterinary Manual. (2025). Contagious ecthyma in sheep and goats. <https://www.msddvetmanual.com/integumentarysystem/poxdiseases/contagiousecthymainsheepandgoats>
- [21]. Kalmus, P., et al. (2024). Retrospective evaluation of udder recovery of cows with subclinical mastitis treated by acoustic pulse technology. Open Veterinary Journal, 14(5), 112. <https://doi.org/10.5455/OVJ.2024.v14.i5.1>
- [22]. Krömker, V., et al. (2021). Noninferiority trial investigating the efficacy of nonsteroidal antiinflammatory drugs and antimicrobial treatment of mild to moderate clinical mastitis. Frontiers in Veterinary Science, 8, 668221. <https://doi.org/10.3389/fvets.2021.668221>
- [23]. Veterinary Paper. (2024). Successful therapeutic management of contagious ecthyma. <https://www.veterinarypaper.com/pdf/2024/vol9issue6/PartI/9684113.pdf>



- [24]. Abutarbush, S. M. (2007). Antiviral activity of HPMPC (cidofovir) against orf virus. *Antiviral Research*, 73(3), 246249. <https://doi.org/10.1016/j.antiviral.2006.10.007>
- [25]. Lacasta, D., Climent, M. J., Pérez, M., Tereso, J. M., & Cabezas, A. (2021). Effect of a topical formulation on infective viral load in lambs naturally infected with orf virus. *Veterinary Research Communications*, 45(3), 145152. <https://doi.org/10.1007/s11259021097854>
- [26]. Veterinary Paper. (2024). Successful therapeutic management of contagious ecthyma. <https://www.veterinarypaper.com/pdf/2024/vol9issue6/PartI/9684113.pdf>
- [27]. Biochem Journal. (2025). Therapeutic management of contagious ecthyma (ORF) in animals. <https://www.biochemjournal.com/archives/2025/vol9issue3S/PartG/S945972.pdf>
- [28]. Comparative therapeutic management of contagious ecthyma in small ruminants. (2016). Academia.edu. https://www.academia.edu/24543075/Comparative_Therapeutic_Management_of_Contagious_Ecthyma_in_Small_Ruminants
- [29]. Sadiq, A. Y., et al. (2017). Severe persistent case of contagious ecthyma (Orf) in goats. *Journal of Animal Health and Production*, 5(1), 2428. https://nexusacademicpublishers.com/uploads/files/JAHP_5_1_2428.pdf
- [30]. MSD Veterinary Manual. (2025). Contagious ecthyma in sheep and goats. <https://www.msddvetmanual.com/integumentarysystem/poxdiseases/contagiousecthymainsheepandgoats>
- [31]. Olde Riekerink, R. G. M., et al. (2022). Incidence of udder cleft dermatitis in Dutch dairy cows. *Journal of Dairy Science*, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>
- [32]. Zigo, F., et al. (2021). Maintaining optimal mammary gland health and preventing mastitis in dairy cows. *Frontiers in Veterinary Science*, 8, 607311. <https://doi.org/10.3389/fvets.2021.607311>
- [33]. CFSPH. (n.d.). Contagious ecthyma factsheet. https://www.cfsph.iastate.edu/Factsheets/pdfs/contagious_ecthyma.pdf
- [34]. Abutarbush, S. M. (2007). Antiviral activity of HPMPC (cidofovir) against orf virus. *Antiviral Research*, 73(3), 246249. <https://doi.org/10.1016/j.antiviral.2006.10.007>
- [35]. Lacasta, D., Climent, M. J., Pérez, M., Tereso, J. M., & Cabezas, A. (2021). Effect of a topical formulation on infective viral load in lambs naturally infected with orf virus. *Veterinary Research Communications*, 45(3), 145152. <https://doi.org/10.1007/s11259021097854>
- [36]. Olde Riekerink, R. G. M., Kelton, D. F., Duffield, T. F., Wever, P., LeBlanc, S., & Keefe, G. (2022). Incidence of udder cleft dermatitis in Dutch dairy cows and risk factors for transitions to udder cleft dermatitis. *Journal of Dairy Science*, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>
- [37]. Zigo, F., Farkašová, Z., Ondrašovičová, S., Zigová, M., Vasil, M., & Kováč, G. (2021). Maintaining optimal mammary gland health and preventing mastitis in dairy cows. *Frontiers in Veterinary Science*, 8, Article 607311. <https://doi.org/10.3389/fvets.2021.607311>
- [38]. CFSPH. (n.d.). Contagious ecthyma factsheet. Iowa State University. https://www.cfsph.iastate.edu/Factsheets/pdfs/contagious_ecthyma.pdf
- [39]. MSD Veterinary Manual. (2025). Contagious ecthyma in sheep and goats. <https://www.msddvetmanual.com/integumentarysystem/poxdiseases/contagiousecthymainsheepandgoats>
- [40]. MSD Veterinary Manual. (2025). Contagious ecthyma in sheep and goats. <https://www.msddvetmanual.com/integumentarysystem/poxdiseases/contagiousecthymainsheepandgoats>
- [41]. Nandi, S., Kumar, M., Manohar, M., & Chander, V. (2011). Current status of contagious ecthyma or Orf disease in goats and sheepA global perspective. *Small Ruminant Research*, 96(1), 7382. <https://doi.org/10.1016/j.smallrumres.2010.11.018>
- [42]. Merck Veterinary Manual. (2025). Contagious ecthyma in sheep and goats. <https://www.merckvetmanual.com/integumentarysystem/poxdiseases/contagiousecthymainsheepandgoats>
- [43]. CFSPH. (n.d.). Contagious ecthyma factsheet. Iowa State University. https://www.cfsph.iastate.edu/Factsheets/pdfs/contagious_ecthyma.pdf
- [44]. Efridi, W., & Haque, A. (2023). Orf viral infection. In *StatPearls*. StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK562191/>



- [45]. CABI Compendium. (2019). Contagious ecthyma (Orf virus).
<https://doi.org/10.1079/cabicompendium.88087>
- [46]. TVMF. (2024). Contagious ecthyma (orf). <https://www.tvmf.org/articles/contagiosecthymaorf/>
- [47]. Olde Riekerink, R. G. M., et al. (2022). Incidence of udder cleft dermatitis. Journal of Dairy Science, 105(7), 62856297. <https://doi.org/10.3168/jds.212254>

