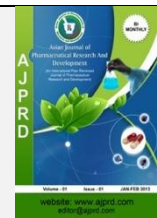


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Review Article

Advancing Therapeutic Horizons: Niosomal Transdermal Drug Delivery for the Management of Lumpy Skin Disease

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ABSTRACT

Lumpy skin disease (LSD) poses a significant threat to the global cattle population, impacting both animal welfare and economic stability in affected regions. Despite various control measures, the disease continues to challenge veterinary professionals. Hypothesis: Exploring the Potential of Niosomal Transdermal Drug Delivery for the Management of Lumpy Skin Disease seeks to examine the promising avenue of utilizing niosomal transdermal drug delivery systems for the treatment of LSD. This review critically analyzes the current understanding of LSD, explores the limitations of conventional treatment approaches and discusses the potential benefits and challenges associated with niosomal transdermal drug delivery in combating this disease.

Keywords: Lumpy skin disease (LSD), Niosomal transdermal drug delivery, Veterinary professionals, Economic stability, Disease management.

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INTRODUCTION:

The multifaceted impact of lumpy skin disease (LSD), a viral infection predominantly affecting cattle, extends beyond its clinical manifestations to encompass significant economic losses and challenges for global livestock farming. Despite its non-zoonotic nature, LSD poses a formidable threat due to symptoms such as fever, skin nodules and lesions affecting various bodily tissues, including the skin, mucous membranes and internal organs.¹ The etiological agent, the LSD virus (LSDV), belonging to the Capripoxvirus genus, underscores its virulence and potential for widespread transmission within cattle populations.² The economic ramifications are profound, including diminished milk production, weight loss, compromised fertility, and mortality in severe cases, which collectively undermine the

economic viability and sustainability of livestock farming enterprises worldwide. In this context, exploring innovative approaches such as niosomal drug delivery systems holds promise for enhancing LSD management strategies. Leveraging the unique properties of niosomes, such as controlled release and enhanced bioavailability, may offer targeted and efficacious therapeutic interventions while minimizing adverse effects and improving treatment outcomes.⁴ Integrating such advanced technologies into LSD management protocols represents a crucial step towards mitigating the disease's impact and safeguarding the livelihoods of livestock farmers globally.

DISEASE PROFILE:^{4,5}

Lumpy skin disease (LSD) in cattle is a viral infection marked by fever, enlarged lymph nodes, and skin nodules, often fatal to immunologically naïve or weak animals. Transmission primarily occurs via blood-sucking insects and can persist in saliva and skin nodules for extended periods. The causative agent, LSD virus (LSDV), belongs to the poxviridae family and is closely related to sheep and goat pox viruses. The virus spreads through animal movement, insect vectors, natural mating and artificial insemination. Risk factors include warm, humid climates favoring vector populations and factors like herd size, migration and trade practices. Symptoms include pain, fever, swollen limbs, reduced milk yield and characteristic nodular skin lesions. Severe cases may lead to blindness, lameness, pneumonia and mastitis, with subclinical infections common. Post-mortem examinations reveal lesions throughout internal organs and pregnant cows may abort. Effective management and biosecurity measures are crucial for control and prevention.

MANAGEMENT:^{6,7}

Traditional approaches to LSD management primarily rely on vaccination, supportive care and symptomatic treatment. However, these methods often exhibit limitations such as the need for repeated injections, potential adverse effects and variable efficacy. Moreover, logistical challenges in vaccine distribution and the emergence of vaccine-resistant strains further complicate disease control efforts.

Primary routes of drug administration in veterinary medicine, mirroring human models, include oral, intramuscular and topical applications like 'pour-on' and 'spot-on' pesticides and antiparasitics (e.g., fenthion, ivermectin). Notably, transdermal delivery, utilizing patches, has gained traction, though limited literature exists in veterinary practice. An understanding of skin anatomy and physiology across species is crucial for effective patch design. Skin structure varies significantly among species, impacting patch design considerations. Skin, a complex organ, plays a vital role in drug absorption, making it imperative to grasp its intricacies for transdermal delivery success. Electrically driven transdermal iontophoretic systems are emerging for controlled peptide drug delivery. The literature on transdermal patches for humans is extensive, underscoring the need for further development and research in the veterinary domain.

TRANSDERMAL DRUG DELIVERY SYSTEM (TDDS):^{8,9}

TDDS administers drugs through the skin for systemic distribution, involving patches, gels, or creams for sustained release.

Components of TDDS:

Drug: Active ingredient with suitable properties for transdermal delivery.

Vehicle: Medium holding the drug, aiding in its stability and release.

Penetration enhancers: Substances facilitating drug permeation through the skin.

Backing film: Protective layer providing structural support to the system.

Release liner: Removable layer covering the adhesive side of the patch.

Mechanism of TDDS:

Involves drug dissolution, penetration, permeation through skin layers, and systemic absorption.

Enhancement strategies for TDDS:

Chemical enhancers, physical methods like sonophoresis and electroporation, and microneedles.

Advantages of TDDS:

Controlled release, improved compliance, avoidance of first-pass metabolism, non-invasiveness, prolonged therapeutic effect, improved safety profile, flexibility in dosage adjustment, improved pharmacokinetics, favorable for drugs with short half-lives, reversible and convenient.

Disadvantages of TDDS:

Limited permeability, skin irritation, slow onset of action, limited dose range, skin permeation variability, limited formulation options, difficulties with lipophilic or hydrophilic drugs, drug-drug interactions, skin integrity limitations and cost.

NIOSOMES:^{10, 11}

Bi-layered structures of non-ionic surfactants, offering versatility in drug encapsulation.

Types of Niosomes: Unilamellar, multilamellar, sponge phase, mannosylated, elastic, ether, pH-sensitive, cationic, stealth.

Factors influencing niosome preparation: Composition, surfactant nature, drug-lipid ratio, hydration medium, preparation method, temperature, additives, polarity of solvent, mechanical agitation, freeze-drying conditions, sterilization methods.

Preparation of Niosomes: Methods include film hydration, reverse phase evaporation, ether injection, microfluidization, handshake method, bubble method, solvent injection, detergent removal, freeze-drying and ethanol injection.

Ingredients and Procedure for Niosomal Patches: Non-ionic surfactant, cholesterol, drug, polymers, plasticizer, organic solvent, distilled water. Procedure involves lipid phase preparation, hydration, drug loading, polymer solution preparation, incorporation of niosomes, casting the film, cutting, packaging and storage.

Applications of Niosomes with Examples: Anti-cancer drug delivery, transdermal drug delivery, vaccine delivery, gene delivery, ocular drug delivery, intranasal drug delivery, cosmetic formulations, diagnostic imaging, nutraceutical delivery, insecticides and pesticides delivery, dermatological applications.

Advantages of Niosomal Transdermal Patches:

Extended drug release, site-specific delivery, enhancement of barrier function.

EXPERIMENTAL EVIDENCE AND CLINICAL IMPLICATIONS:

The efficacy of many products is enhanced by penetration enhancers, modifying the skin barrier for drug delivery. Skin, specialized in various species, acts as a protective barrier while permitting life functions. Advances in transdermal drug delivery expand therapeutic options, with more drugs reaching

systemic circulation through the skin. Veterinary products achieve benefits despite the skin's protective functions. Success in this field is due to understanding the skin barrier's structure and function. Incorporating vehicles or compounds in transdermal systems helps overcome skin barriers. Substances like alcohols and glycols act as penetration enhancers, improving drug transport. However, their use raises concerns about adverse reactions and tissue residues. Veterinary drugs often utilize penetration enhancers for topical delivery. Species variation in skin anatomy affects drug absorption, demanding tailored approaches. Hair follicles serve as important pathways for drug absorption, especially in animals. Understanding species differences is crucial for effective transdermal drug delivery in veterinary medicine. The skin's architecture forms an effective barrier, necessitating penetration enhancers for drug delivery. Despite research efforts, finding ideal penetration enhancers remains a challenge, balancing efficacy and safety. Initial penetration enhancers, like aprotic solvents, had limitations due to toxicity and irritancy.

Table 1: Experimental Evidence for patches for animals:¹²⁻²¹

Application	Example	Species	Purpose/Use
Fentanyl patches	Pain management	Dogs, cats	Post-operative pain relief, chronic pain management
Hormonal patches	Reproductive management	Zoo animals	Regulating estrus cycles, fertility management
Transdermal methimazole	Hyperthyroidism treatment	Cats	Alternative to oral medication, ease of administration
Transdermal scopolamine	Motion sickness prevention	Dogs	Alleviating motion sickness during travel
Pheromone patches	Stress reduction	Dogs, cats	Calming effect, behavior modification
Transdermal antibiotics	Antibiotic therapy	Various species	Treating localized skin infections, wound care
Transdermal anti-inflammatory	Pain management	Dogs, cats	Managing arthritis, inflammation
Transdermal chemotherapy	Cancer treatment	Horses	Targeted drug delivery for certain cancers
Vitamin/mineral supplementation	Nutritional support	Various species	Meeting dietary needs, exotic species in captivity
Transdermal flea/tick control	Parasite prevention	Dogs, cats	Preventing infestations
Transdermal anesthesia	Sedation	Fish	Aquaculture procedures, surgery
Transdermal vaccination	Disease prevention	Wildlife	Vaccination campaigns, conservation efforts
Transdermal glucose monitoring	Diabetes management	Various species	Continuous monitoring of blood glucose levels
Transdermal anti-parasitic drugs	Parasite control	Livestock	Controlling internal/external parasites

SUMMARY:

The introduction delves into lumpy skin disease (LSD), a viral infection impacting cattle globally, causing significant economic losses and posing multifaceted challenges to

livestock farming. LSD, primarily transmitted through blood-sucking insects, manifests with fever, nodules and lesions on the skin, mucous membranes and internal organs, severely affecting cattle health and productivity. Traditional

management approaches, including vaccination and supportive care, are limited by efficacy, logistical hurdles and emerging vaccine-resistant strains. Transdermal drug delivery systems (TDDS), particularly niosomes, emerge as promising avenues for LSD treatment, offering controlled release, site-specific delivery, and enhanced barrier function. However, the translation of niosomal transdermal drug delivery into clinical practice requires optimization of formulation parameters, rigorous safety evaluations and validation through clinical trials, underscoring the necessity for further research to address these challenges and advance therapeutic horizons in LSD management. Despite its potential, niosomal transdermal drug delivery for LSD presents several challenges that warrant further investigation:

Optimization of Formulation Parameters: Fine-tuning of niosomal composition, size and surface characteristics is necessary to maximize drug encapsulation efficiency and skin permeation.

Evaluation of Safety Profile: Comprehensive preclinical studies are needed to assess the safety and biocompatibility of niosomal formulations, particularly regarding long-term use and potential immunogenicity.

Translation to Clinical Practice: Clinical trials are essential to validate the efficacy, safety and feasibility of niosomal transdermal drug delivery in real-world settings, considering factors such as dose optimization, treatment duration and patient variability.

CONCLUSION:

The exploration into the potential of niosomal transdermal drug delivery for managing lumpy skin disease (LSD) underscores its transformative impact on addressing therapeutic challenges associated with this viral infection in cattle. Despite the need for further research to overcome existing hurdles and validate preclinical findings in clinical settings, the integration of niosomal technology presents a promising avenue for revolutionizing LSD management strategies and safeguarding global livestock health. By offering controlled release, site-specific delivery and enhanced barrier function, niosomal transdermal drug delivery systems hold the potential to significantly improve treatment outcomes while minimizing adverse effects and logistical constraints associated with traditional management approaches. Continued investment in research and development efforts aimed at optimizing niosomal formulations, evaluating safety profiles and conducting clinical trials will be crucial for realizing the full therapeutic potential of this innovative approach in combating LSD and enhancing the resilience of livestock farming worldwide.

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