Indian J Anim Health (2024)
DOI: https://doi.org/10.36062/ijah.2024.09024

Review Article

Ethnoveterinary approach in Lumpy Skin Disease (LSD): A review

S. Palai[1], S. S. Kesh[2*] and S. Biswas[3]

[1]Department of Veterinary Pharmacology and Toxicology, College of Veterinary Science and Animal Husbandry, Odisha University of Agriculture and Technology, Bhubaneswar- 751 003, Odisha, India; [2]Department of Veterinary Clinical Complex (Veterinary Biochemistry), Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata- 700 037, West Bengal, India; [3]Department of Veterinary Biochemistry, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata- 700 037, West Bengal, India

Abstract

Research on treatments and cures for Lumpy Skin Disease (LSD) has significantly grown in India, where the condition is growing increasingly. The main focus of drug repurposing research is on conventional treatments. The disease is characterised by the skin's eruption of nodules covering the entire body of the affected animal. The lesions are seen in the upper respiratory tract and mouth. Anorexia, pneumonia, pyrexia and dysgalactia are among the systemic effects. The disease causes loss to the farmer due to declined milk production, abortions, infertility, permanent damage to the hides, and occasional death. However, most of the antiviral drugs are synthetic small molecules, and antiviral plant-derived medicines are yet to be discovered for LSD. The treatment of LSD with ethnoveterinary medicinal formulations has been suggested by the National Dairy Development Board (NDDB). It included plants with various bioactive compounds having antioxidative, anti-inflammatory, immunomodulatory, analgesic, and antiviral properties. These ethnoveterinary medicinal formulations are proven superior when used singly or in combination with existing drugs to enhance the effectiveness of antivirals and increase their bioavailability. The use of medicinal plants and their phytochemicals would relieve the suffering in animals. It can also be the right path for the creation of new affordable drugs through scientific studies.

Keywords: Cattle, LSD, Medicinal plants, Phytochemicals

Highlights

- The Lumpy Skin Disease affects cattle and water buffaloes leading to substantial economic repercussions.
- The characteristic nodular lesion may slough and form holes that may subsequently be attractive to screwworm flies and bacteria with chances of septicaemia.
- Following the widespread of LSD, NDDB advised the use of plant-based immune stimulants, appetite stimulants, and fly repellents.
- Some plants are beneficial in reducing LSD symptoms owing to their natural antioxidant, anti-inflammatory, immunomodulatory and antiviral effects.
- To protect animals against LSD, the use of natural products under the guidance of veterinary professionals should be encouraged.

INTRODUCTION

Millions of families worldwide, particularly in developing nations, rely heavily on the livestock industry for their daily needs. However, the effects of several infectious diseases and natural calamities are most felt by rural households who depend on agriculture and cattle (Saqib *et al*., 2023). The Lumpy Skin Disease (LSD) is an infectious disease caused by a virus of the Capripoxvirus genus and Poxviridae family affecting Buffalo (*Bubalus bubalis*) and cattle (*Bos taurus* and *Bos indicus*). The *Bos taurus* is more vulnerable than native varieties of cattle. The disease results in considerable financial losses to cattle-rearing farmers due to declined milk production, abortions, infertility, permanent damage to the hides, and occasionally death (Jatav, 2022). Clinical signs of a mild infection include one or two nodular lumps after the onset of ocular discharge, fever, emaciation, and agalactia. Later, these itchy and painful nodular lesions appear on the skin of the back, lower ear, legs, tail, muzzle, nares, scrotum, perineum, eyelids and oral mucosa. The disease is carried by arthropod vectors directly as well as indirectly through animals sharing troughs, milk, saliva, blood, nasal and lachrymal

*Corresponding Author, E-mail: keshvbc@gmail.com

secretions (Goud and Vijaykumar, 2020). The disease has a higher morbidity and lower mortality, causing a net economic loss. This newly discovered viral illness lowers animal productivity and raises management expenses in cattle. Many nations have experienced the dangerous consequences of LSD (Chouhan *et al*., 2022).

Since there is no direct treatment for Lumpy Skin Disease in cattle, antibiotics such as ceftiofur, sulphonamides, enrofloxacin, or penicillin with streptomycin (Dicrysticin) can be used to treat secondary bacterial infections; anti-inflammatory medications such as meloxicam, analgin (Vetalgin) or ketoprofen can be used to reduce fever and pain; and antihistamines, electrolytes, and immunity enhancers can be used to manage the symptoms in infected animals. Together with liquid feed, soft feed, fodder, or succulent pasture, skin lesions or nodules can be treated with wound care sprays, antiallergic, and antiseptic ointments.

Since the current antiviral medications are synthetic, expensive, and have side effects, this pressing issue inspired the current review paper to promote the ethnoveterinary approach to Lumpy Skin conditions. The farmer can lessen their financial burden by using these plant-based medications, which can help treat affected cattle and prevent non-affected cattle from getting sick. This article will highlight the efficacy of plant-based drugs for their further research and development in the effective treatment and prevention of LSD.

Plant secondary metabolites have more chance of interaction with other biological molecules and exhibit better biological activity than synthetic small molecules (Atanasov *et al*., 2021). Various plants advised by the National Dairy Development Board (NDDB) are recommended for topical or oral use in LSD which are rich but underutilised sources of antiviral bioactive compounds. These plants secondary metabolites are safer and cheaper than synthetic compounds. The most recent research concentrates on isolating them, synthesising their analogues, and examining how they affect health by utilising various methods in animal models (Ullah *et al*., 2020). To better understand the nature and impacts of plant secondary metabolites, we have made an effort to summarise plant and their phytochemicals effective against the Lumpy Skin Disease virus (LSDV). This article aims to help students, researchers and drug developers to discover safer and cheaper plant-based antiviral drugs against LSD with more efficacy against drug resistance too. This article will also help field veterinarians to understand and prescribe the herbal treatment for animals suffering from LSD.

Epidemiology

Although LSD epidemic outbreaks are often seasonal, they can happen at any time since no season is entirely free of vectors in affected countries. Large-scale LSD outbreaks are typically caused by the presence of an increasing number of susceptible animals, plenty of active blood-sucking vectors, and unrestrained movement of animals. The main instance is frequently connected to new animals introduced into a herd or close proximity to a new animal. Mortality rate is typically around 10%, and morbidity ranges from 2 to 45%. The host's susceptibility is influenced by immunological function, age, and breed. Typically, cows with high milk production suffer the most (Tuppurainen *et al*., 2017).

Aetiology and virus ecology

Lumpy Skin Disease is a highly contagious, WOAH-marked transboundary poxvirus infection of the bovine species carried by a vector (Parvin *et al*., 2022). The Lumpy Skin Disease virus has its place under the genus Capripox virus and family Poxviridae causing Lumpy Skin Disease. The sheep and goat pox viruses are phylogenetically different but closely related to the Lumpy Skin Disease virus as they have the same genus. LSDV is an oval- or brick-shaped virus with a length of 294±20 nm and width of 262±22 nm with a bilateral body covered by a bilipid bilayer. This huge, double-stranded DNA virus has very little genetic diversity and is highly stable. There are nine more LSDV genes that are unique to cattle infections and are not active in SPPV and GTPV (Akther *et al*., 2023).

Transmission

The knowledge of the numerous LSDV transmission methods and regional vector species could help to stop the disease's early progress and, hence, stop widespread transboundary dispersion. Arthropod transmission is the most likely way that the LSDV virus transmits, as evidenced by the seasonality of outbreaks associated with warm and rainy weather. The vast majority of the time, animal migrations are linked to the long-distance spread of LSDV. Numerous dipteran pests like flies that affect cattle provide the basis for the spread of the LSDV. As outbreaks can occur despite the apparent absence of vectors, showing that there are additional routes of transmission, such as fomite transmission via animal trough sharing, milk, saliva, blood, nasal, and lachrymal

secretions, can also help spread of LSDV. Veterinarians could create more effective, scientifically based containment and preventative strategies against LSDV (Sprygin *et al*., 2019).

Host range

The virus that causes Lumpy Skin Disease is highly host-specific; it only affects bovine species like cattle and water buffalo; other domesticated species including sheep, goats, pigs, and horses are not impacted (Azeem *et al*., 2022). Although the morbidity rate is substantially lower in Asian water buffalo (*Bubalus bubalis*) (1.6%) than in cattle (30.8%), Lumpy Skin Disease is host-specific and causes spontaneous infection in animals. Sheep and goats are capable of reproducing some LSDV strains. Although specific antibodies for LSDV have been found in a variety of wild ruminants, including blue wildebeest, eland, giraffe, impala, and greater kudu, whenever experimental inoculation has been conducted, cattle are still the definitive hosts (Kumar *et al*., 2021). Human beings are not affected by Lumpy Skin conditions. Nevertheless, to predict potential host jump, it is important to regularly observe and monitor disease outbreaks and virus mutations (Pal and Gutama, 2023).

Clinical findings

About 50% of vulnerable calves who become infected experience lacrimation, fever, nasal discharge, and hypersalivation before developing the typical body flare-ups. The time of incubation of LSDV is 4 to 14 days. The entire cutis as well as the mucosa of the GI, respiratory, and vaginal systems are affected by the nodules, which are well-circumscribed, spherical, somewhat elevated, painful, and firm. Nodules can form on the oral and nasal mucous membranes and muzzle. A solid, creamy-grey or yellow mass of tissue is present in the skin nodules. Regional lymph nodes swell and oedema forms in the legs, udder and brisket. Sometimes, a secondary infection develops and leads to significant sloughing and suppuration, resulting in emaciation and death. The nodules either regress at that point or necrosis of the skin results in "sit-fasts", which are hard, raised patches that are unique from the surrounding skin. These areas flake off, leaving scarring ulcers that recover (Fig. 1). The biggest loss occurs as a result of loss of condition, decreased milk production, decreased value of the hide, or rejection (Mulatu and Feyisa, 2018).

Diagnosis

Clinical diagnosis is the main method for diagnosing LSD, which is subsequently backed up by PCR analysis of lesion crusts or biopsies of the affected nodules or skin, virus isolation, and histology of affected areas. However, LSDV infection is not always visible because mild and subclinical illness may manifest. Even after cattle are experimentally infected,

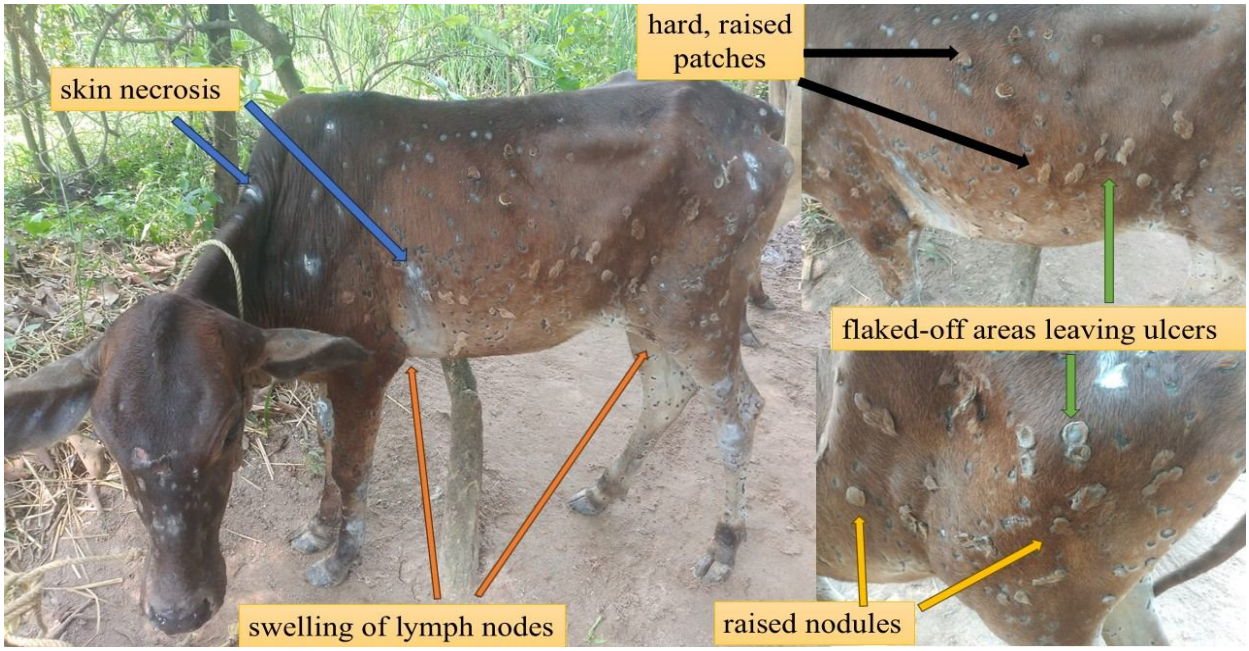

Fig. 1. A clinical case of LSD showing its typical clinical signs

up to 50% of the animals are found still uninfected or only sub-clinically sick.

The condition could be confused with the herpesvirus-caused pseudo-lumpy skin disorder, which has little clinical significance (bovine herpesvirus 2). Although the herpesvirus lesions appear to be limited to the teats and udder of cows in bovine herpes mammillitis, both diseases can be clinically identical. The difference between pseudo-Lumpy Skin Disease and actual Lumpy Skin Disease is mainly determined by the isolation and/or identification of the causative virus. Electron microscopy can show the poxvirus in the early skin lesions of Lumpy Skin Disease. PCR can tell the two illnesses apart (Aerts *et al*., 2021). Clinical symptoms of LSD can be mistaken for those of other conditions such as foot and mouth disease, insect bite, demodicosis, and hypersensitivity.

Treatment

Unfortunately, the Lumpy Skin Condition/Disease cannot yet be treated with any specific antiviral medication. Symptomatic and supportive care for cattle is the sole treatment by using anti-inflammatory medications for inflammatory conditions, paracetamol for high fevers, antihistamine medications for allergic conditions, and antibiotics for secondary bacterial infections (Babiuk, 2018).

Control and prevention

The lack of effective treatments for the Lumpy Skin Disease virus highlights the need for effective immunisation for disease prevention. To control LSD, a live attenuated vaccine is available. The sheep pox and goat pox vaccines can be used to treat LSD because the two viruses are closely related. It may be possible to stop the disease from spreading by immunisation and enforcing strict quarantine rules and vector control measures.

Restricting the movement of animals having LSD infection and placing animals with lesions in quarantine are effective control and prevention measures for the disease. The disease can also be prevented by limiting and controlling vector movement. It is advised to feed livestock with liquid feed, soft feed, and succulent pasture (Gupta *et al*., 2020).

Ethnoveterinary medicinal approach for LSD management

The situation needs the rapid discovery of new preventative and therapeutic drugs. The NDDB along with the Institute of Transdisciplinary Health Science and Technology has advised the use of medicinal plants and their products as traditional herbal preparations after significantly increased spread of LSD. Strong fly-repellent properties in some herbal sprays, creams, and gels prevent flies from resting on wounds and stop maggots from entering wounds. These properties also promote rapid wound repair in skin nodules due to rapid collagenisation. Herbal appetite stimulants help animals maintain their body condition by restoring their appetite and rumen functions. Immunity is strengthened, and overall health is improved by plant-based immune modulators and antioxidants. Some organic energy boosters help keep an animal's energy level up and active.

Exploring the ethnoveterinary medicinal approach to Lumpy Skin Disease

Phytochemicals are derived from plants and serve a variety of reproductive and protective roles in plants, including odour, colour, and hormone functions involved in growth and expansion. These are the secondary metabolites of plants widely present in fruits, nuts, whole grains, vegetables and seeds. These terpenoids, lipids, carbohydrates, alkaloids, phenolics, and other nitrogen-containing substances are frequently created in response to environmental cues like illness, nutrient deficiencies, and climatic changes. Approximately 4000 phytochemicals have been discovered so far. Phytochemicals are extensively used in a wide range of *in-vivo* and *in-vitro* models that reveal their therapeutic effects against various diseases (Behl *et al*., 2021).

A vast range of phytochemicals have shown promise as antiviral agents in numerous epidemiological and experimental studies. A variety of *in-vitro* and *in-vivo* investigations employing various biological assays have been used to identify a number of intriguing leads, particularly in the last ten years. The infinite range of chemical components found in medicinal plants can be used to combat genetic and invasion divergence, and so prevent the proliferation of DNA and RNA viruses. In reality, the field of ethnopharmacology enhances the likelihood of discovering a novel therapeutic candidate (Watson *et al*., 2010).

In the LSD outbreak, the NDDB recommended the use of herbal treatment where numerous plants are used as oral and topical preparations. Two oral formulations have been recommended, and every dose needs to be made fresh each time from herbs. Two topical herbal formulations are advised for both ordinary and maggoted wounds (Table 1). These plants or herbs containing various phytochemicals possess antioxidant, anti-inflammatory, analgesic,

immunomodulatory and antiviral activity (Table 1). Investigations of these medicinal plants can assess their impact on Lumpy Skin Disease. Some of these compounds may be analysed through modern biology with a wide range of disciplines and sophisticated techniques for isolation, characterisation and evaluation. The most recent research also concentrates on synthesising their analogues, and examining how they affect health utilising a range of methods and animal models. The successfully isolated phytocompounds will be further evaluated for their pharmacological properties to determine the most potent natural compounds that can be utilised as anti-LSD drugs in a short amount of time (Ullah *et al*., 2020).

Table 1. Medicinal plants useful for the management of Lumpy Skin Disease

Sl. No.	Name and family of the plant used	Part used	Phytochemicals	Beneficial effects observed *in vivo/ in vitro*	Reference
1.	*Acalypha indica* (Indian copper leaf) Muktajhuri, Shwetbasanta Family:Euphorbiaceae	leaves, stem, flowers, roots and seeds	retusoquinone, swietenine, cephalotaxine, octadecanoicacid	laxative and antiparasitic, emetic, expectorant, laxative and diuretic, free radical scavenging/ antioxidant and anti-inflammatory properties	Sahukari *et al*., 2021
2.	*Aegle marmalos* (Bilva/bel)Bela Family: Rutaceae	fruits	aegeline, marmelosin, aegelenine, myrecetin, aegelinosides, marmelin, marmelide	antibacterial, anti-ulcerative colitis, hepatoprotective, antiviral, antidiarrheal, gastroprotective, radioprotective, antidiabetic, and cardioprotective effects	Manandhar *et al*., 2018
3.	*Allium cepa* variety aggregatum (Shallots) Gundhun Family: Amaryllidaceae	bulbs	quercetin, gallic, kaempferol allicin, diallyl disulphide, s-allylcysteine, diallyl trisulfide	antioxidative and anti-inflammatory, antibacterial, antiviral and antidiabetic effects	Ounjaijean *et al*., 2019
4.	*Allium sativum* (Garlic)Rasoon Family: Amaryllidaceae	bulbs	s-allylcysteine, s-allylmercapto-cysteine	antioxidant,cardioprotective, immunomodulator, anti-thrombotic and anti-inflammatory effects	Chandra *et al*., 2023
5.	*Annona muricata* (Soursop) Lakshmanfal Family: Annonaceae	leaf paste	anonaine, annonamine, muricine, stepharine, genistein	anxiolytic, anti-inflammatory, contraceptive, antioxidant, anti-tumoral, antimicrobial, anti-inflammatory, insecticide, larvicide, and antiulcer activity	Coria-Téllez *et al*., 2018
6.	*Azadirachta indica* (Neem)Nim/ Nimba Family: Meliaceae	leaves	azadirachtin, nimbin, azadirachtin, gedunin, and nimbolide, nimbidine	microbicidal, hypoglycemic, hepatoprotective, antipyretic, insecticidal, antidiabetic, anti-inflammatory, antioxidant, and antileishmaniasis properties	Wylie and Merrell, 2022
7.	*Cinnamomum verum* (cinnamon) Dalchini Family: Lauraceae	bark	cinnamyl acetate, cinnamic acid, cinnamaldehyde, eugenol, caryophyllene,	cytotoxic, anticancer, antidiabetic, antioxidant, antimicrobial, anti-inflammatory, and wound-healing effects	Singh *et al*., 2021

Cont. Table 1.

Table 1., Cont. ...

Sl. No.	Name and family of the plant used	Part used	Phytochemicals	Beneficial effects observed *in vivo/ in vitro*	Reference
8.	*Cocos nucifera* L. (Coconut) Narikel/ Nariyel Family: Arecaceae	oil	lauric acid and alpha-tocopherol, oleic acid, α-linolenic acid	analgesic, antibacterial, antipyretic, antihypertensive, anti-inflammatory, antimicrobial, and antioxidant, effects	Dehuri *et al*., 2021
9.	*Coriandrum sativum* (Coriander)Dhaniya Family: Apiaceae	seeds	linalool, limonene, camphor, geraniol	antimicrobial, anti-inflammatory, antiulcerogenic, anti-hepatotoxic and tonic agent	Palai and Rudrapal, 2023
10.	*Cuminum cyminum* (Cumin) Jeera Family: Apiaceae	dried seeds	p-cymene, gamma-terpinene, phenyl glycol, l-β-pinene,	antioxidant, antimicrobial, anticancer, antioxidant, antiscleriotic, and immunomodulatory effect	Behbahani *et al*., 2019
11.	*Curcuma longa* (Turmeric)Halud/ Haldi Family: Zingiberaceae	rhizomes	curcumin demethoxycurcumin, curcumenol, curcumol, eugenol	antioxidant, antiviral, antibacterial, anti-inflammatory, hepatoprotective, antiseptic, and cardioprotective actions	Chanda and Rama-chandra, 2019
12.	*Ocimum basilicum* (Sweet basil)Tulsi Family:Lamiaceae	leaves	caffeic, rosmarinic acid, quercetin, rutin, apigenin, vanillic, rosmarinic acids, α-pinene, β-pinene, methyl chavicol, 1,8 cineole	hepatoprotective, antibacterial, anti-stress immunomodulatory, antidiabetic, antipyretic, antioxidant, hypolipidemic, anti-inflammatory, and antihyperglycemic actions	Shahrajabian *et al*., 2020
13.	*Piper betel*(Betel) Pan patta Family: Piperaceae	leaves	betal-phenol, chavicol, eugenol, quercetin	antimicrobial, antiallergic, wound healing, antioxidant, antiseptic, bactericidal, antiviral, radioprotective, antifungal, anti-inflammatory, antiplatelet, antibacterial, and immunomodulatory activity	Palai *et al*., 2021
14.	*Piper nigrum* (Black pepper) Gol Marich Family: Piperaceae	fruits	sabinene, limonene, 3-carene, α-pinene, caryophyllene	antioxidant, anti-inflammatory, antidiabetic, antimicrobial, gastroprotective, and insecticidal activity	Ashokkumar *et al*., 2021
15.	*Saccharum officinarum* L. (Sugarcane) Ganna/ aakhu Family: Poaceae	evaporated juice	apigenin, tricin, luteoline, orientin, vitexin, tricin, schaftoside, swertisin	antioxidants, cytoprotective, aphrodisiac, laxative, cooling, demulcent, antiseptic, and anthelmintic action	Senthilkumar *et al*., 2024
16.	*Sesamum indicum* L. (Sesame)Rashi/ Til Family: Pedaliaceae	oil	sesamin, sesaminol, gamma tocopherol, cephalin, lecithin	antioxidant, antibacterial, antifungal, antiviral, anti-inflammatory and antiproliferative activities	Kesh and Palai, 2021
17.	*Swertia chirayita* (Chirata) Chirayeta Family: Gentianaceae	leaf powder	seco-iridoid glycosides (swertiamarin), oleanolic acid	neuroprotective, anticonvulsant, anxiolytic, hepatoprotective antioxidant, anthelmintic, antibacterial, antihepatitic, anti-leishmanial action	Kshirsagar *et al*., 2019

Fig. 2. Several important medicinal plants for the management of Lumpy Skin Disease

Activities of plants and their phytochemicals effective against Lumpy Skin Disease (LSD)

Many whole plants, nuts, fruits, vegetables, bark and leaves contain phytochemical molecules with likely antiviral, anticancer, antioxidant, and anti-inflammatory actions (Fig. 2). In medical chemistry, finding the most prevalent components in any kind of extract is typically the first step in examining the biological activity of complex natural products, including their antiviral properties. This method helps in choosing compounds for additional research against viruses.

Antioxidant activity: Reactive oxygen species (ROS) are mostly produced by-products of the electron transport chain in the human body. They are essential for the immune system, differentiation, apoptosis, and protein phosphorylation activities. Oxidative stress is the result of ROS interacting with substances like lipids, proteins, or nucleic acids. Cellular membranes are harmed by lipid peroxidation brought on by ROS. The osmotic pressure and membrane potential of the cell are altered as a result of membrane damage, which results in cell death. The body's defence system uses processes of enzyme inhibition of nitric-oxide synthase and xanthine oxidase activity to counteract endogenously elevated ROS. Phytochemicals directly oxidise radicals to create less reactive species through the modification of channel pathways and interactions with other enzyme systems (Brunetti *et al*., 2013) like quercetin, which improves vascular health and lowers the risk of cardiovascular disease. Plants with antioxidant capabilities include *Sesamum indicum* and *Allium cepa* (Amiri *et al*., 2019). The leaf extract's antioxidant activity and radical-scavenging capacity are strongly connected with its flavonoid and phenolic content (Das *et al*., 2019). The DPPH (2, 2-diphenyl-1-picryl-hydrazyl-hydrate) assay can be used to evaluate the antioxidant effects of phytochemicals such as dihydrochalcone, chalcone, flavanone, flavanol, flavonol and flavone.

Anti-inflammatory activity: The intricate process of inflammation continues to be vital to the host's defence. Chronic diseases may develop as a result of excessive inflammatory mediator production. The study of plants having inflammatory properties can be done with plant extracts that exhibit anti-inflammatory properties at various stages of the inflammatory process, preventing eicosanoids and cytokines production, initiation of inflammatory reaction cascade and reducing itching, flareup, extreme exfoliation, etc. (Oguntibeju, 2018). The anti-inflammatory properties of therapeutic plants occur through a variety of modes of action.

Prostaglandins, thromboxanes and leukotrienes are produced as a result of phospholipase A2 releasing

arachidonic acid from membrane lipids, which is a precursor to eicosanoids. Inflammatory disorders can be effectively treated and managed by blocking the COX and LOX pathways in the arachidonic cascade with any medicinal drug that inhibits phospholipase. Quercetin, which inhibited human neutrophils, was the first flavonoid to be found to inhibit phospholipase A2. Some of the medicinal herbs, such as *Allium sativum*, *Curcuma longa* and *Allium cepa* inhibit phospholipase A2 (Giresha, 2021).

The LOX family of enzymes includes lipoxygenases involved in many inflammatory diseases. 15-LOX is a crucial isomeric enzyme needed in leukotrienes production from arachidonic acid. As biologically active leukotrienes are intermediaries of numerous pro-inflammatory and allergy reactions, inhibiting leukotriene production by 15-LOX is regarded as one of the healing alternatives in the supervision of inflammatory diseases (Ananthi *et al*., 2010). Plant flavonoids can reduce the expression of iNOS by inhibiting nitric oxide formation. Also, flavone and flavones with amino substitutes prevent the generation of NO (Krol *et al*., 1995). The flavonoid class of polyphenols can prevent prostaglandin formation. There are two isomeric versions of COX (COX-1 and COX-2) that are widely present in inflammation. Many anti-inflammatory herbal extracts and phytochemicals target COX-1 and COX-2 inhibition (Nworu and Akah, 2015).

Different pro-inflammatory cytokines control inflammatory responses either directly or indirectly, stimulating the production of other cytokines or cellular adhesion molecules in specific cell types. The suppression of pro-inflammatory cytokines is reported after feeding plant extracts high in flavonoids to rats (Rahman *et al*., 2022).

Plants, herbs and their phytoconstituents primarily influence the numerous protein kinases tangled in signal transduction, such as protein kinase C and mitogen-activated protein kinase. The DNA-binding ability of transcription factors like nuclear factor-kappa B and activator protein-1 is controlled by the inhibition of these enzymes, which in turn affects the expression of the target gene (Cooper *et al*., 2007).

Immunomodulatory activity: The nuclear factor (NF)-kB, an oxidant-induced transcription factor that is clinically significant for the production of the immunodeficiency virus gene, is inhibited by these phytochemicals. These guard DNA from changes and harm caused by free radicals. They offer defence against UV- and ionising-radiation-caused immunosuppression. Treatment with both Gallic and ellagic acids significantly reduced the Leishmania major-induced infection of macrophages. Additionally, Gallic and ellagic acide improve immunological responses by increasing nitrite release, phagocytosis and lysosomal volume (Alves *et al*., 2017).

Piper longum increases bone marrow cellularity, WBC count, and general antibody production. Piperinoate found in *P. longum* improved Th1/Th2 cytokine imbalance, showing anti-tumour action in RAW 264.7 cells and mouse erythrocyte model. Additionally, piperine inhibits IL-2 and INF-γ production during peripheral blood mononuclear cells cell proliferation. The treatment with vanillic acid, chlorogenic acid, aucubin, ferulic acid, and p-coumaric acid greatly increases lymphocyte proliferative activity and IFN-γ production (Sunila and Kuttan, 2004).

Antiviral activity: The wide range of active phytochemicals have therapeutic applications against various viruses with different genetic makeups and functions. These substances' antioxidative properties, scavenging abilities, suppression of DNA and RNA synthesis, blocking of viral replication, etc. help them work against viruses. The host cell environment is a necessity for the survival of viruses. Divergent invasion tactics can present a significant barrier in addition to genetic heterogeneity. The bioflavonoid, myricetin, has an excellent antiviral effect against the hepatitis B virus and influenza virus (Ren and Song, 2005).

The bioactivity of molecules is largely due to this coordinating capacity. The plant pigments called anthocyanidins have a free OH group that can coordinate with metal ions like Ca^{2+} and Mg^{2+} in an alkaline environment. Anthocyanidin is effective in treating viral illnesses (Andersen *et al*., 1997). Naringin is used to treat viral infections such as HCV, HIV, picornaviruses, and respiratory viruses. Human immunodeficiency virus and related immunodeficiency virus infections were found to be more effectively inhibited by flavan-3-o1. Epigallocatechin 3-O-gallate and samarangenin B reported the most powerful inhibitory activity on Herpes Simplex Virus (HSV)-1 reproduction of all the substances tested for this purpose in Vero cells (Lin *et al*., 2000). Incorporation of rosmarinic acid into a phospholipid combination showed success in treating HSV infection (Bunyapraphatsara *et al*., 2000; Loizzo *et al*., 2008).

Conclusion

The development of medicine candidates from

diverse traditional, alternative, and complementary therapies is now receiving more attention all over the world. Phytochemicals found in plant extracts can be used to scientifically develop novel medications owing to the presence of natural and bioactive components effective against the Lumpy Skin Disease virus. The phytochemicals obtained from medicinal plants with anti-antioxidant, anti-inflammatory, immuno-modulatory, and antiviral properties can be employed for LSD treatment. Exploring the antiviral components found in medicinal plants will aid in creating novel natural anti-LSD medications.

Conflict of interest: There is no conflict of interest in the study.

Author's contributions: SSK: Conception of the work; SP: Designing of the work; SP, SSK: Drafting of the article; SB: Critical revision of the article; SSK, SP, SB: Final approval of the version.

REFERENCES

Aerts L, Haegeman A, De Leeuw I, Philips W, Van Campe W *et al*., 2021. Detection of clinical and subclinical Lumpy Skin Disease using ear notch testing and skin biopsies. Microorganisms, 9(10): 2171, doi: 10.3390/microorganisms9102171

Akther M, Akter SH, Sarker S, Aleri JW, Annandale H *et al*., 2023. Global burden of Lumpy Skin Disease, outbreaks, and future challenges. Viruses, 15(9): 1861, doi: 10.3390/v15091861

Alves MM, Brito LM, Souza AC, Queiroz BC, de Carvalho TP *et al*., 2017. Gallic and ellagic acids: two natural immunomodulator compounds solve infection of macrophages by *Leishmania major*. Naunyn Schmiedebergs Arch Pharmacol, 390(9): 893-903, doi: 10.1007/s00210-017-1387-y

Amiri M, Jelodar GA, Erjaee H and Nazifi S, 2019. The effects of different doses of onion (*Allium cepa*. L) extract on leptin, ghrelin, total antioxidant capacity, and performance of suckling lambs. Comp Clin Path, 28: 391-396, doi: 10.1007/s00580-019-02910-5

Ananthi S, Raghavendran HR, Sunil AG, Gayathri V, Ramakrishnan G *et al*., 2010. *In vitro* antioxidant and *in vivo* anti-inflammatory potential of crude polysaccharide from *Turbinaria ornata* (Marine Brown Alga). Food Chem Toxicol, 48(1): 187-92, doi: 10.1016/j.fct.2009.09.036

Andersen OM, Helland DE and Andersen KJ, 1997. Anthocyanidin and anthocyanidin derivatives, and their isolation, for treatment of cancer, diseases caused by lesions in connective tissues, and diseases caused by viruses. PCT Int Appl, 121

Ashokkumar K, Murugan M, Dhanya MK, Pandian A and Warkentin TD, 2021. Phytochemistry and therapeutic potential of black pepper [*Piper nigrum* (L.)] essential oil and piperine: A review. Clin Phytosci, 7: 52, doi: 10.1186/s40816-021-00292-2

Atanasov AG, Zotchev SB, Dirsch VM and Supuran CT, 2021. Natural products in drug discovery: advances and opportunities. Nat Rev Drug Discov, 20(3): 200-216, doi: 10.1038/s41573-020-00114-z

Azeem S, Sharma B, Shabir S, Akbar H and Venter E, 2022. Lumpy Skin Disease is expanding its geographic range: A challenge for Asian livestock management and food security. Vet J, 279: 105785, doi: 10.1016/j.tvjl.2021.105785

Babiuk S, 2018. Treatment of Lumpy Skin Disease. In: Lumpy Skin Disease. Springer, Cham, pp 81-81, doi: 10.1007/978-3-319-92411-3_17

Behbahani BA, Noshad M and Falah F, 2019. Cumin essential oil: phytochemical analysis, antimicrobial activity and investigation of its mechanism of action through scanning electron microscopy. Microb Pathog, 136: 103716, doi: 10.1016/j.micpath.2019.103716

Behl T, Kumar K, Brisc C, Rus M, Nistor-Cseppento DC *et al*., 2021. Exploring the multifocal role of phytochemicals as immunomodulators. Biomed Pharmacother, 133: 110959, doi: 10.1016/j.biopha.2020.110959

Brunetti C, Di Ferdinando M, Fini A, Pollastri S and Tattini M, 2013. Flavonoids as antioxidants and developmental regulators: relative significance in plants and humans. Int J Mol Sci, 14(2): 3540-3455, doi: 10.3390/ijms14023540

Bunyapraphatsara N, Dechsree S, Yoosook C, Herunsalee A and Panpisutchai Y, 2000. Anti-herpes simplex virus component isolated from *Maclura cochinchinensis*. Phytomedicine, 6(6): 421-424, doi: 10.1016/S0944-7113(00)80069-0

Chanda S and Ramachandra TV, 2019. Phytochemical and pharmacological importance of turmeric (*Curcuma longa*): A review. RRJoP, 9(1): 16-23

Chandra S, Palai S, Fagner Ferreira-Matias E, Cavalcante Pita-Neto I, Lucas Gomes-Ramalho CERO *et al*., 2023. Indian medicinal plants are effective in the treatment and management of COVID-19. Biocell, 47(4): 677-695, doi: 10.32604/biocell.2023.026081

Chouhan CS, Parvin MS, Ali MY, Sadekuzzaman M, Chowdhury MGA *et al*., 2022. Epidemiology and economic impact of Lumpy Skin Disease of cattle in Mymensingh and Gaibandha districts of Bangladesh. Transbound Emerg Dis, 69(6): 3405-3418, doi: 10.1111/tbed.14697

Cooper SJ and Bowden GT, 2007. Ultraviolet B regulation of

transcription factor families: roles of nuclear factor-kappa B (NF-κappaB) and activator protein-1 (AP-1) in UVB-induced skin carcinogenesis. Curr Cancer Drug Targets, 7(4): 325-34, doi: 10.2174/156800907780809714

Coria-Téllez AV, Montalvo-Gónzalez E, Yahia EM and Obledo-Vázquez EN, 2018. Annona muricata: A comprehensive review on its traditional medicinal uses, phytochemicals, pharmacological activities, mechanisms of action and toxicity. Arab J chem, 11(5): 662-691

Das S, Ray A, Nasim N, Nayak S and Mohanty S, 2019. Effect of different extraction techniques on total phenolic and flavonoid contents, and antioxidant activity of betelvine and quantification of its phenolic constituents by validated HPTLC method. 3 Biotech, 9(1): 1-8, doi: 10.1007/s13205-018-1565-8

Dehuri M, Palai S, Mohanty B and Malangmei L, 2021. Anti-helminthic activity of plant extracts against gastrointestinal nematodes in small ruminants- A review. Pharmacogn Rev, 15(30): 117-127, doi: 10.5530/phrev.2021.15.14

Giresha AS, 2021. Secretory Phospholipase A2 Group IIA: A Potential Therapeutic Target in Inflammation. Current Research and Trends in Medical Science and Technology, 1: 34-85

Goud KS and Vijayakumar K, 2020. Lumpy Skin Disease in large ruminants-an emerging threat. Intas Polivet, 21(1): 1-8

Gupta T, Patial V, Bali D, Angaria S, Sharma M *et al*., 2020. A review: Lumpy Skin Disease and its emergence in India. Vet Res Commun, 44(3): 111-118, doi: 10.1007/s11259-020-09780-1

Jatav M, 2022. Chapter-4 Lumpy Skin Disease (LSD): An Emerging Trans-Boundary Viral Disease. Advances in Veterinary Sciences, 16: 39-50

Kesh SS and Palai S, 2021. Roles of medicinal plants in the treatment of connective tissue diseases. In Phytochemistry, the Military and Health, Elsevier, pp 353-366, doi: 10.1016/B978-0-12-821556-2.00027-X

Krol W, Czuba ZP, Threadgill MD, Cunningham BD and Pietsz G, 1995. Inhibition of nitric oxide (NO.) production in murine macrophages by flavones. Biochem Pharmacol, 50(7): 1031-1035, doi: 10.1016/0006-2952(95)00237-t

Kshirsagar PR, Jagtap UB, Gaikwad NB and Bapat VA, 2019. Ethnopharmacology, phytochemistry and pharmacology of medicinally potent genus Swertia: An update. S Afr J Bot, 124: 444-83, doi: 10.1016/j.sajb.2019.05.030

Kumar P, Kumari RR, Devi S, Tripathi MK, Singh J *et al*., 2021. Emergence and transboundary spread of Lumpy Skin Disease in South Asia. Indian J Anim Sci, 91 (7): 507-517, doi: 10.56093/ijans.v91i7.115893

Lin LC, Kuo YC and Chou CJ, 2000. Anti-herpes simplex virus type-1 flavonoids and a new flavanone from the root of *Limonium sinense*. Planta Med, 66(4): 333-336, doi: 10.1055/s-2000-8540

Loizzo MR, Saab A, Tundis R, Statti GA, Lampronti I *et al*., 2008. Phytochemical analysis and *in vitro* evaluation of the biological activity against herpes simplex virus type 1 (HSV-1) of *Cedrus libani* A. Rich. Phytomedicine, 15(1-2): 79-83, doi: 10.1016/j.phymed.2007.03.013

Manandhar B, Paudel KR, Sharma B and Karki R, 2018. Phytochemical profile and pharmacological activity of *Aegle marmelos* Linn. J Integr Med, 16(3): 153-163, doi: 10.1016/j.joim.2018.04.007

Mulatu E and Feyisa A, 2018. Review: Lumpy Skin Disease. J Vet Sci Technol, 9(535): 1-8

Nworu CS and Akah PA, 2015. Anti-inflammatory medicinal plants and the molecular mechanisms underlying their activities. Afr J Tradit Complement Altern Med, 12: 52-61, doi: 10.4314/ajtcam.v12i6.3S

Oguntibeju OO, 2018. Medicinal plants with anti-inflammatory activities from selected countries and regions of Africa. J Inflamm Res, 11: 307-317, doi: 10.2147/JIR.S167789

Ounjaijean S, Chachiyo S, Kulprachakarn K, Boonyapranai K, Srichairatanakool S *et al*., 2019. Antioxidant and anti-inflammatory protective properties of Thai shallot (*Allium ascalonicum* cv. Chiangmai) juice on human vascular endothelial cell lines (EA. hy926). Walailak J Sci Technol (WJST), 16(3): 175-184, doi: 10.48048/wjst.2019.6222

Pal M and Gutama PK, 2023. Can Lumpy Skin Disease be considered a zoonosis? Am J Infect Dis Microbiol, 11: 13-17, doi: 10.12691/ajidm-11-1-3

Palai S and Rudrapal M, 2023. Functional Foods, Herbal Supplements and Nutraceuticals in the Management of Coronavirus Disease-2019 (COVID-19). In: Medicinal Plants, Phytomedicines and Traditional Herbal Remedies for Drug Discovery and Development against COVID-19. Bentham Science Publishers, pp 200-218

Palai S, Kesh SS, Awuchi CG, Abdulrahman, SA and Egbuna C, 2021. Role of Phytochemicals in the Treatment of Ectoparasitic Infections: Scabies and Myiasis. In: Neglected Tropical Diseases and Phytochemicals in Drug Discovery, pp 477-498

Parvin R, Chowdhury EH, Islam MT, Begum JA, Nooruzzaman M *et al*., 2022. Clinical epidemiology, pathology, and molecular investigation of Lumpy Skin Disease outbreaks in Bangladesh during 2020-2021 indicate the re-emergence of an old African strain. Viruses, 14(11): 2529, doi: 10.3390/v14112529

Rahman MM, Mim SA, Tumpa MA, Sarker MT, Ahmed M *et al*., 2022. Exploring the management approaches of cytokines including viral infection and neuroinflammation for neurological disorders. Cytokine, 157: 155962, doi: 10.1016/j.cyto.2022.155962

Ren Q and Song X, (2005). Use of a composition containing dihydromyricetin and myricetin in preparation of antiviral

medicines. Faming Zhuanli Shenqing Gongkai Shuomingshu, 20: 33

Sahukari R, Punabaka J, Bhasha S, Ganjikunta VS, Kondeti Ramudu S *et al*., 2021. Phytochemical profile, free radical scavenging and anti-inflammatory properties of *Acalypha Indica* root extract: evidence from *in vitro* and *in vivo* studies. Molecules, 26(20): 6251, doi: 10.3390/molecules26206251

Saqib SE, Yaseen M, Visetnoi S, Sikandar and Ali S, 2023. Epidemiological and economic consequences of Lumpy Skin Disease outbreaks on farm households in Khyber Pakhtunkhwa, Pakistan. Front Vet Sci, 10: 1238771, doi: 10.3389/fvets.2023.1238771

Senthilkumar S, Kuppusamy S, Baskar M, Vijayalatha KR, Jayavalli R *et al*., 2024. Cultivating tomorrow: A review on biostimulants and their transformative role in agriculture. J Adv Biol Biotechnol, 27(8): 906-919, doi: 10.9734/jabb/2024/v27i81211

Shahrajabian MH, Sun W and Cheng Q, 2020. Chemical components and pharmacological benefits of Basil (*Ocimum basilicum*): A review. Inter J Food Prop, 23(1): 1961-1970, doi: 10.1080/10942912.2020.1828456

Singh N, Rao AS, Nandal A, Kumar S, Yadav SS *et al*., 2021. Phytochemical and pharmacological review of *Cinnamomum verum* J. Presl- A versatile spice used in food and nutrition. Food Chem, 338: 127773, doi: 10.1016/j.foodchem.2020.127773

Sprygin A, Pestova Y, Wallace DB, Tuppurainen E and Kononov AV, 2019. Transmission of Lumpy Skin Disease virus: A short review. Virus Res, 269: 197637, doi: 10.1016/j.virusres.2019.05.015

Sunila ES and Kuttan G, 2004. Immunomodulatory and antitumor activity of *Piper longum* Linn. and piperine. J Ethnopharmacol, 90(2-3): 339-346, doi: 10.1016/j.jep.2003.10.016

Tuppurainen E, Alexandrov T and Beltrán-Alcrudo DJ, 2017. Lumpy Skin Disease- A Manual for Veterinarians. FAO Animal Production and Health Manual, 20

Ullah A, Munir S, Badshah SL, Khan N, Ghani L *et al*., 2020. Important flavonoids and their role as a therapeutic agent. Molecules, 25(22): 5243, doi: 10.3390/molecules 25225243

Watson RR, Zibadi S and Preedy VR, 2010. Dietary Components and Immune Function. Springer Science and Business Media

Wylie MR and Merrell DS, 2022. The antimicrobial potential of the neem tree *Azadirachta indica*. Front Pharmacol, 13: 891535, doi: 10.3389/fphar.2022.891535

Received- 09.07.2024, Accepted- 03.11.2024, Published- 06.12.2024 (Online)
Section Editor: Dr. C. K. Jana, Section Editor