

The devastation of Lumpy skin disease in third world countries: a mini – review on the current status of the disease focusing phytochemicals

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ABSTRACT: Lumpy skin disease is a rising bovine viral illness that is widespread in most African and Middle Eastern nations, with a high probability of disease transmission throughout the Asia and Europe. The causative agent is capripoxvirus endangering hundreds of dairy cattle across the country in recent years. The LSD virus infects cattle and buffaloes and results in nodular skin sores all over their bodies. This results in chronic debility, decreased milk supply, poor development, infertility, abortion, and other issues in cattle and buffaloes infrequently leading to death of animals. The only infected animal species are cattle and water buffalo, both of which have high morbidity and low mortality rates. However, mortality rates are greater in calf populations. LSD causes sterility in males and abortions in female cattle. This mini review highlights existing information on epidemiology, pathogenesis, clinical manifestations, and potential role of phytochemicals particularly turmeric and aloe vera in treating lumpy skin disease.

Keywords: Lumpy skin disease; phytochemicals; Endemic; Asia, antibiotics alternatives

1. INTRODUCTION

Lumpy skin disease is an emerging fatal threat to domestication and livestock, characterized by nodular lesions on skin with high mortality rate. The causative agent of lumpy skin is capripoxvirus, containing a double stranded DNA (dsDNA) of 150kbp. This dsDNA encodes 30 structural or nonstructural homologues of poxviral proteins, lipid envelope, and a total diameter of having of about 260-320nm (Namazi and Khodakaram Tafti, 2021).

For the first time this disease was observed in the in Africa and in the Middle East after which it started to spread to south-east Europe, the Caucasus, Russia, and most recently to Asia. There are also some studies witnessing the prevalence of the disease in Russian Federation, Cyprus, and Greece. The recent epidemic in Asia has considerably affected the economy in terms of reduced productivity of animals and their export (Flannery et al., 2022). It now poses a threat of spreading among all countries and may soon reach Australia. The disease's primary

mode of transmission is most commonly through insect vectors like biting flies or mosquitoes although transmission via direct or indirect contact is possible (Shumilova et al., 2022). Typical skin lumps and a high fever are regarded as major indications, and clinical manifestations of the illness include anorexia, infertility, early embryonic death, decreased milk production, and infertility. On examination, nodules are frequently seen on the mucosa of the oropharynx, udder, genitalia, and rectum (Khan et al., 2021). Currently no antiviral medications available to treat lumpy skin condition. Supportive care for cattle is the only kind of treatment that involves using wound care sprays, antibiotics, anti-inflammatory pain killers and intravenous fluid administration. The ability of phytochemicals to influence a wide range of molecular pathways while being less harmful and more useful has recently gained traction. Phytochemical combinations induce apoptosis, limit cell invasion and metastasis, target malignant cells, and strengthen the immune system Rizeq, B., Gupta, I., Ilesanmi, J., AlSafran, M., Rahman, MD.M., Ouhtit, A. (2020). The Power of Phytochemicals Combination in Cancer Chemoprevention. *Journal of Cancer*, 11(15), 4521-4533. <https://doi.org/10.7150/jca.34374>.

Phytochemicals are plant derived nutrients and are present in almost all dietary sources, phytochemicals are also termed as phytonutrients, phytobiotics, phytochemical. Much effort has gone into developing antibiotic alternatives to preserve or enhance poultry health and productivity (Windisch et al., 2008). Phytochemicals can be both spices and herbs, however they can be administered as solid, dried, crushed, or extracts (crude or concentrated) forms (Applegate et al., 2010). Polyphenols are the primary bioactive compounds are a major class of phytochemicals; their concentration and composition vary depending on the type of plant, its parts, its geographical origin, the time of year it is harvested, its environment, how it is stored, and the methods used in its processing Gadde, U., Kim, W., Oh, S., & Lillehoj, H. (2017). Alternatives to antibiotics for maximizing growth performance and feed efficiency in poultry: A review. *Animal Health Research Reviews*, 18(1), 26-45. doi:10.1017/S1466252316000207. Mechanism of action of phytochemicals depends on the attributes of the active ingredients present. The potential of phytochemicals to impose beneficial effects are majorly due to antioxidant, anti-inflammatory, and immuno-modulatory

properties (Kim et al., 2015). The purpose of this study is to investigate potential role of several classes of phytochemicals in treating skin conditions, and beneficial roles of curcumin and aloe vera in treating or managing lumpy skin disease in animals.

LSD is caused by the infectious capripoxvirus virus which enters through the skin or GIT mucosa, followed by viremia and a violent response (Saminathan et al., 2020). The infection then spreads to nearby lymph nodes, causing inflammation. The virus replicates in endothelial cells present in lymphatic and blood vessels, causing both regional and systemic reactions leading to vasculitis and lymphadenitis (Ahmed et al., 2020). While in severe conditions edema, necrosis, thrombosis and other symptoms may be observed which produces an epitheliotropic condition (Raja et al.). LSD nodules can turn grey pink with caseous necrotic centers while confined necrotic lesions may ulcerate however skin localization is brought on by the LSDV's epitheliotropic feature. Gammada I, Morshed MM, Rabby TR, and Hossain MI. (2022). The prevalence of lumpy skin disease in the cattle population: a brief study. *Int. J. Agric. Vet. Sci.*, 4(3), 55-67.

The necrotic cores, often known as "sit-fasts," detach from the surrounding skin, while within these necrotic cores, swollen lymph nodes and consequent bacterial infections are common. During infection, several virus-encoded components are produced which have an impact on disease etiology (Aldayel, 2019). Histopathological examination of affected cattle showed dermal nodules that were 2-5 cm in size, well-confined, spherical, slightly elevated, and hard. The center area of the nodules had significant necrosis of the epidermal and dermal layers, and considerable infiltration of mononuclear inflammatory cells such as macrophages and lymphocytes were also observed. Furthermore, widespread and severe vasculitis was seen, keratinocytes had eosinophilic intracytoplasmic inclusion bodies, perifollicular edema and phagocytosed tissue debris was also observed (Kamr et al., 2022).

In most cases, lesions appear with biphasic fever and incubation period lasts about two to four weeks (Gammada et al.). Clinical findings usually include intermittent fever, excessive drooling, nasal congestion, appetite loss, hypersalivation, however skin eruptions include round, hard nodules found all over the body (Abutarbush et al., 2015). These skin nodules

affects both dermal and epidermal layers, however edema affects the limbs and associated tissues, and enlargement of superficial lymph nodes occur. Secondary bacterial infections are frequent which may worsen the illness (Delhon, 2022). The affected animals are frequently debilitated, and pregnant cows may abort, the intensity of the sickness is determined on the viral strain and breed of cattle. i.e. Domestic cattle (*Bos taurus*) are more prone than zebu cattle (*Bos indicus*) (Fenin et al.). In severe cases continuous high pyrexia (40-41.5°C), lethargy, and anorexia may occur. A significant economic loss will then result from decreased milk supply, abortions, temporary or permanent sterility, damage to hides, and fatalities (Feyisa, 2018). Lesions range from mild to severe. The mild one is only observed in young cattle with two to three lumps over body and the detached lumps may leave an ulcer after two days of onset of fever (Hasib, 2020). Painful nodules in diameter of 1 to 5 cm appear on skin with depression and anorexia (Salib and Osman, 2011). Most common site of nodules in animal body are back, legs, scrotum, perinium, eyelids, nasal and oral mucosa, lower ear, and tail (Al-Salihi and Hassan, 2015). While the severe form is observed both in young and aged cattle. The complications of the severe form includes persistent fever of (40-41.5°C) for two weeks and numerous intradermal lumps (up to hundreds) are found which vary both in size and location i.e. subcutaneous or intramuscular lumps, while in some cases unilateral or bilateral keratitis, umbilicus with oozing pus, and swelling of face and legs has been observed, as a consequence recovered animals require more time to return to their usual state. Incidence of lumpy skin disease among Egyptian cattle in Giza governorate, Egypt - F. A. Salib, A. H. Osman.

2. Significance of the components of phytochemicals in viral infections

No treatment for lumpy skin disease, caused by capripoxivirus has been recommended yet. However, to cope with the secondary bacterial infections, fever, inflammation, and to increase the animal's appetite, antibiotics, and anti-inflammatory medicines along with vitamins are often administered i.e. (a) In order to cover up nutritional deficiencies, the immune system is boosted up by administering supplements. (b) Iodides are given to maintain thyroid function which help in sustaining the body growth and metabolism. (c) To control LSDV spread attenuated vaccines are administered that has

proven effective in controlling the spread. (d) Autohemotherapy to increase circulating macrophages in body therefore helps fight infective agents. (e) Use of nanotechnology is a new approach in treatment of LSD (f) Use of phytochemicals in treating skin diseases caused by any etiology (Veterinary and N B, 2022).

Phytochemicals are characterized as bioactive nutritional plant compounds found in fruits, vegetables, grains, and other plant foods. Due to their positive impacts on human health and significant health benefits for consumers, phytochemicals are of great interest and have significant antioxidant potential (Jimenez-Garcia et al., 2018). Skin is the first line of defence against environmental stresses such as ultraviolet (UV) radiation, which can cause dermatological problems like early aging, aberrant pigmentation, and inflammatory responses. There are well-established positive and negative impacts of UV radiation on human health (Chaiprasongsuk and Panich, 2022). Skin diseases constitute about 34% of all ailments and are supposed to be the most common disease among rural people. Since AIDS/HIV has been linked to skin illnesses, they have received more attention. More than 90% of HIV-positive individuals experienced mucosal and skin issues at some point during the illnesses. Herbal medicine is an alternative therapy for the treatment and control of skin ailments (Halder et al., 2012).

Phytochemicals are bioactive non-nutrient components of plants that are typically present in human diet and are beneficial to mankind and animals (Wiseman, 2013). Phytochemicals have traditionally been used to treat a variety of ailments, and they have also been shown to decrease viral replication/transcription. Most of them prevent viruses from entering the host cell or from replicating, phytochemicals that inhibit viral genome have the antioxidant activity. Furthermore, the antiviral properties of plant-based medicines for developing viral infections have been studied. Due to their lower toxicity, plant-based antiviral natural chemicals are the most suitable and effective alternative to antiviral agents, inhibitors, and medications (Ghildiyal et al., 2020).

2.1 Curcumin

Curcumin (*Curcuma Longa*) is a polyphenol obtained by the rhizomes of turmeric. Curcumin is a cytoprotective chemical, and its efficacy and safety have been proven in cell-based and animal

investigations (Gupta et al., 2017). Exploring its effectiveness in conditions including skin cancers, colon, duodenal, pancreatic, breast, and other skin illnesses at higher doses is attractive. Curcumin protects the skin by inhibiting nuclear factor-KB and quenching free radicals. Curcumin treatment also accelerates wound healing time, and enhanced collagen deposition (Thangapazham et al., 2007). The turmeric spice contains a yellow pigment called curcumin (diferuloylmethane), which has been linked to anti-inflammatory, anti-cancer, antiviral, and antibacterial properties, it also possesses chemosensitizing, chemopreventive, radiosensitizing activities (Prasad et al., 2014). Curcumin has been used for the treatment of the following skin conditions:

Psoriasis: About 3% of the world's population is affected by this multifactorial, multisystemic, chronic inflammatory disease. Uncontrolled proliferation of keratinocytes, activation of inflammatory cytokines and dendritic cells results in formation of thick silvery plaques thereby the excessive generation of TNF- by activated macrophages can be reduced by curcumin. Curcumin is also the active non-competitive inhibitor of phosphatase kinase (Aggarwal et al., 2013). In animal studies, daily applications of 1% curcumin gel reduced cutaneous psoriasis-like inflammation through the blockage of potassium channels (subtypes Kv1.3) expressed in T cells and the elimination of IL-17A, IL-17F, IL-22, and such other pro-inflammatory cytokines in mouse ear samples. Notably treatment of 100 μ M curcumin decreased the growth of T cells and inflammatory cytokines by more than 50% (Kang et al., 2016). In human studies, Compared to other conventional topical treatments, curcumin 1% alcoholic gel plaques showed reduced keratinocyte transferrin receptor (TRR) expression, parakeratosis severity, and epidermal CD8+ T cell density (Herman and Herman, 2016). Turmeric tonic substantially reduced cutaneous symptoms when compared to the placebo, and it also enhanced the patient's quality of life (Bahraini et al., 2018).

Atopic Dermatitis

Atopic dermatitis is a persistent, itchy, inflammatory skin condition that is brought on by a complex interaction of immunological, environmental, and genetic factors. Atopic dermatitis is the most common chronic inflammatory skin disease, pathogenesis is not yet fully understood but is theorised as a complex

interaction of skin barrier alteration and immune weakness (Kim et al., 2019). Curcumin is traditionally used in Asian countries for the treatment of atopic dermatitis (Gupta et al., 2013).

Iatrogenic dermatitis: Iatrogenic dermatitis is a general term used to describe a number of inflammatory skin disorders that can be directly linked to the use of drugs or medical treatments. Typical examples are radiation induced and applied medication induced dermatitis. In animal studies, daily topical administration of curcumin improved epithelial cell survival and recovery in radiation-damaged skin by lowering the expression of nuclear factor-B and cyclooxygenase-2 -kappaB (Kim et al., 2016). In human studies, oral treatment of curcumin (4 g/day) prevented the hand-foot syndrome (HFS) brought on by capecitabine (Scontre et al., 2018).

Lumpy skin disease: LSD is a vector borne disease of cattle and water buffaloes in Asia. Affected cattle suffers from lump and necrotic masses all over the body, with typical vasculitis and lymphadenitis (Sprygin et al., 2019). Curcumin has been reported to enhance cattle immunity, and alleviate inflammation, moreover anti-proliferative activity of curcumin has proven to be a treatment strategy for devastating illness of LSD in cattle (Jantan et al., 2015; Khafagi et al.). Curcumin along with 112 more phytochemicals have been proven to possess anti-viral properties, which has been demonstrated to be efficient against numerous viruses including LSD (Oluwale Oladosu et al., 2021). Due to its potential benefits, mostly from its anti-inflammatory and antioxidant characteristics, curcumin has been used as a traditional treatment for any form of skin condition for centuries. Topical application of curcumin was reported efficient in treatment of lumpy skin disease, however the entire treatment consisted of administration of Enrofloxacin at dose rate of 10mg per animal, Meloxicam at dose rate of 0.5mg/kg of body weight, and antihistamines as a combination therapy (Vinothraj et al., 2020). In another case study, combination therapy of ethovetirinary medicine and conventional medicine was implemented. Ethovetirinary medicine consisted of curcumin powder, neem leaves, garlic, custard apple leaves and basil leaves mixed in coconut oil on external lesions applied topically for fifteen days, and a mixture of betel leaves, black pepper and jaggery was prepared into a paste and administered orally for fifteen days, while conventional therapy

consisted of Amoxirum forte per kg of body weight, 0.1 mg of Meloxicam per kg of body weight, 1.5 million units of Vit A, 15 ml of Tribivet, and 1000 ml of DNS regularly for five days. This combination therapy was proven efficient on animal as it showed signs of recovery on day three, and after fifteen days of treatment, the animal was completely recovered with improved skin health, wound healing, no scars or wounds were left, and lumps didn't formed ulcers/abscesses in entire fifteen days of treatment (Yadav et al., 2021). In another research study of LSD infection, curcumin powder along with thirteen more phytonutrients were orally administered and topically applied regularly for two weeks. Potentially beneficial roles of all phytonutrients were proven a treatment of LSD infection in cattle (Islam, 2022; Yadav et al.).

2.2 Resveratrol

Resveratrol is a natural polyphenolic phytoalexin belongs to a class of stilbenes present in Japanese knotweed red grapes, red wine, berries and peanuts and has been proven to have antioxidant, cardioprotective, neuroprotective, chemopreventive and pharmacological effects against variety of diseases, including skin conditions. It has a potential to protect skin from oxidative stress of UV radiation, skin cancer and other inflammatory skin hyper-proliferative disorders (Ndiaye et al., 2011). Resveratrol is effective in the treatment of several skin disorders such as acne, exfoliative eczema, and psoriasis. However, due to its short biologic half-life and low oral absorption, which limit its favourable therapeutic effects, topical administration is a feasible strategy in the management of a variety of dermatological conditions (Gugleva et al., 2020). In animal studies, topical application of oxy-resveratrol for cutaneous HSV-1 infection was observed in Balb/c mouse, therapeutic effects of resveratrol showed viral inhibitions by 26% -33% in the infected vero cells within 3 – 6 hours of application. Resveratrol combination with acyclovir produced synergic response against HSV-1 virus. Topical administration of resveratrol ointment (30%) for five times in a day delayed the development of cutaneous lesion caused by HSV-1 (Lin et al., 2021). In human studies, resveratrol topical treatment significantly reduced the number of facial acne lesions in acne vulgaris patients at concentration of 1mg/g of total preparation. The study did not clarify whether resveratrol's therapeutic effect on acne vulgaris derives from its antibacterial or

anti-inflammatory effects (Vestergaard and Ingmer, 2019).

2.3 Quercetin

Quercetin is a naturally occurring polyphenol flavonoid commonly present in citrus fruit, buck wheat, onions that has antioxidant properties. Quercetin plays an important role in anti-allergic, anti-inflammatory and immunomodulatory functions, making it suitable for the treatment of a variety of disorders, and is been traditionally used for variety of diseases, such as chronic inflammation, cardiovascular diseases, nervous disorders and obesity (Zhang et al., 2011).

Quercetin is one of the major flavonoid human diet and human body needs upto 40mg of daily uptake (Jafarinia et al., 2020). Recent clinical research points to quercetin as a potential all-natural cure for inflammatory skin conditions. Recent years have seen significant significant advances in the understanding of the molecular processes underlying quercetin's anti-AD effects (Karuppagounder et al., 2016). In animal studies, quercetin anti-inflammatory action on atopic dermatitis like lesions were examined for 8 days, histological examination reduced the expression of inflammatory mediators, which played potentially beneficial role in controlling atopic dermatitis symptoms (Hou et al., 2019).

2.4 Aloe vera

Aloe vera (Aloesin) is a succulent plant that thrives in the desert and subtropical areas. It is utilized in Ayurvedic, Homoeopathic and Allopathic systems of medicine for medical benefits. It has been applied to reduce perspiration, oral dosage for diabetes and to get rid of a range of gastrointestinal ailments. The leaves of this amazing medicinal plant are rich in various bioactive compounds that have emollient, purgative, anti-inflammatory, antioxidant, anti-microbial, anti-fungal, anti-helminthic, antiseptic and cosmetic properties. They also contain large amount of vitamins, minerals, natural sugars, enzymes and amino acids (Lanka, 2018). Aloe vera's ability to heal wounds, prevent ulcers and speed up the recovery from cutaneous injuries and skin infection, aloe vera had greater efficacy than gauze dressing with petroleum jelly and cream containing framycetin (Hekmatpou et al., 2019). It suppresses the release of immunosuppressive cytokines originating from skin keratinocytes and prevent the UV-induced suppression of delayed type hypersensitivity. Aloe vera inhibits

the growth of some micro-organisms particularly gram-positive bacteria that causes food poisoning and illness in humans (Stanley et al., 2014).

Aloe vera gel contain anti-inflammatory properties that not only reduce pain and discomfort but also hasten the healing properties. It also showed anti-inflammatory potential for the treatment of H. Pylori infection (Sánchez et al., 2020). The most prevalent skin condition that bothers adolescents and adult is acne and aloe vera has an excellent anti-acne properties and works against any type of skin irritation (Saleem et al., 2022). Plant-based therapies have a distinct place in medicine because of their powerful advantages and lack of adverse effects. Antibiotics are used to treat bacterial illnesses and enhance the health of animals, but their rising overuse is creating a severe threat to animal health because of emergence of antibiotic resistance (Ayukekbong et al., 2017).

Aloe vera is gaining popularity due to its abundance of nutrients such as polysaccharide, antioxidant and amino acids. It enhance the health and welfare of animals due to their natural antibacterial properties by maintaining positive balance of gut microflora (Buttar et al., 2022). Since aloe vera has beneficial potential to treat skin diseases due to all properties mentioned above, it's efficacy in treatment of LSD is known and proven. The neethling variant of lumpy skin disease virus causes microscopic lesions in cattle that include a granulomatous reaction in the dermis and hypodermis that spread to surroundings tissue leading to necrosis, and edema (Annandale, 2020). Hence treatment of LSD was recently made possible through aloe vera which involved use of other phytonutrients along with it. A herbal cocktail was made out of baking soda neem leaves, curcumin powder, aloe vera jelly, pepper and garlic for fourteen days regularly, also affected animals were regularly washed with neem water that lead to good results with complete recovery of animals from LSD infection (Yadav et al., 2021).

3. Medicinal value of aloe vera in livestock

The primary plant components utilized to make aloe-based herbal treatments that frequently targeted cattle (29.3%) and poultry/chickens (28.2%) were the leaves (65.4%) and the whole plant (4.7%) (Aremu and Lawal, 2022). Aloe vera is becoming more popular since it has a wealth of nutrients that are good for human health, including vitamins, minerals,

polysaccharides, phytosterols, antioxidants, and amino acids (El-Sayed and El-Sayed, 2020). The state of the health and welfare of livestock are enhanced. Aloe vera has antibacterial ability, which is attributable to the presence of anthraquinones, has the potential to prevent animal illness from the gel extracts, isolated. Aloe vera includes antiseptic substances that have restrictive effect against bacteria, fungi, virus (Buttar et al., 2022). The animal intestinal micro flora is significantly improved by phytoextracts. Numerous research utilizing herbal extracts alternative to antibiotic in the form of additives direct or indirect impact on gut (Garcia et al., 2007).

Aloe vera polysaccharides were found to boost Lactobacillus and Bifidobacterium while decreasing the amount of E.coli (Niko, 2016). Aloe vera is a well-known plant with antibacterial, anti-inflammatory, anti-tumor, anti-fungal, wound healing properties that are antioxidant and anti-diabetic. Numerous factors affect the causes of abomasa ulcers in cattle. Inappropriate eating practices that result in stress-causing gastrointestinal disturbances or it could be negative effect of using non-steroidal and anti-inflammatory medicine (Adhikari et al., 2017). Due to Aloe vera as a feed additive in livestock, aloe vera juice has been shown to be useful against ulcers and many digestive diseases (Aremu and Lawal, 2022). Various phytonutrients and their mechanistic review are various skin conditions is briefly shown in **Table 1**.

4. Expert opinion

The threatful lumpy skin disease is a cattle viral disease manifested by severe losses affecting naïve animals. It has remained an endemic in Middle East, Africa and currently in Asian countries. Also, it is transmitted directly or indirectly and such transmission is facilitated by mechanical vectors. It has been observed that the infection free areas were suffered due to infected vectors and animals.

Furthermore, the lumpy skin disease virus transmission was reduced by the whole – herd culling infected farms. As no suitable treatment options are available for LSD however; attenuated vaccines are available to cope with the worse consequences. Among such vaccines the homologous vaccines are considered more significant than sheep pox vaccines. It shows a clear-cut need for the development and improvement of vaccines that differentiate the vaccinated and infected animals. In addition, an awareness campaign is required for veterinary

personals and farmers as well to help in recognition of LSD viruses. Finally, curcumin has shown therapeutic potential in the treatment of LSD traditionally and it along with other

phytonutrient needs exploration in order to open new horizons in the treatment of Lumpy skin disease.

Skin Conditions	Phytonutrients used	Mechanism	Effects	References
Psoriasis	Curcumin	Non competitive and selective inhibition of phosphorylase kinase, Down-regulation of pro-inflammatory cytokines, Up-regulation of involucrin and filaggrin, Inhibition of potassium channels	Anti-proliferative effect, Inhibits growth of psoriatic like cells, Enhanced skin barrier function, Anti-inflammatory effect	(Kang et al., 2016; Reddy and Aggarwal, 1994; Varma et al., 2017)
	Resveratrol	Inhibition of transcription factor NF- κ B	Anti-inflammatory effect	(Kjær et al., 2015)
		Activation of sirtuin enzyme	Inhibition of cell differentiation Regulation of cell cycle Minimizes over-expression of cytokines	(Elgewelly et al., 2022)
	Quercetin	Inhibition of Th17 cell differentiation Stimulation of Nrf2 signal	Significant reduction of (PASI) scores Reduction in temperature of lesions	(Wang and Wang, 2019)
		Blockade of NF- κ B, IKK α , NIK, JAK/STAT3 pathways Stimulation of TRAF3	Anti-inflammatory effect Reduction in histopathology's progression Anti-oxidant	(Chen et al., 2017)
	Aloevera	Inhibition of TNF - α	Anti-inflammatory effect	Leng H, Pu L, Xu L, Shi X, Ji J and Chen K: Effects of aloe polysaccharide, a polysaccharide extracted from Aloe vera, on TNF- α -induced HaCaT cell proliferation and the underlying mechanism in psoriasis. Mol

				Med Rep 18: 3537-3543, 2018
Lumpy skin disease	Curcumin	Blockade of NO production, NF- κ B, (COX-2) and (iNOS), Direct inhibition of viral replication and cellular signalling pathways	Anti-inflammatory effect Immune- modulation, Anti- viral effect	(Jantan et al., 2015; Mathew and Hsu, 2018)
	Aloevera	Direct interference with envelop of virus , and dsDNA genome	Antiviral effect	(Yagi et al., 2020)
	Neem leaves	Blockade of NF- κ B, p53, pTEN, VEGF, bcl2, bax	Wound healing Anti-inflammatory effect Regulation of apoptotic process	(Alzohairy, 2016)
		Regulation of pro- inflammatory cytokines	Anti-inflammatory effect	(Alzohairy, 2016)
	Betel leaves	Blockade of COX-1 and COX-2	Anti-inflammatory effect	(Yadav et al.)
		Blockade of catalase, dismutase, and peroxidase	Anti-oxidant effect	(Rathee et al., 2006)
	Garlic	Activation of NOS	Immune system modulation	(Sasi et al., 2021)
Atopic dermatiditis	Curcumin	Blockade of NF- κ B, and MAPK	Anti-oxidant effect Anti-inflammatory effect	(Sharma and Naura, 2020)
		Activation of Nrf2	Allergic response suppressed	(Sharma and Naura, 2020)
Eczema	Curcumin	Blockade of TNF	Anti-inflammatory effect	(Khiljee et al., 2011)
		Fat epithelization	Wound contraction and healing	(Khiljee et al., 2011)
	Aloevera	Activation of adiponectin	Improved blood circulation	(Boudreau and Beland, 2006)
		Increase O ₂ transportation Angiogenesis	Stops cells death	(Kim et al., 2010)

	Oats	Suppression of pro-inflammatory cytokines	Anti-inflammatory effect Anti-oxidant effect	(Michelle Garay et al., 2015)
	Chamomile	Transcription activation Adipogenesis	Skin cell regeneration Anti-oxidant	(Solanki, 2011)

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