Artykuł przeglądowy *Review*

Digital dermatitis in cattle: Emphasis on non-antibiotic treatment methods

PAULINA KAŹMIERCZAK[1], GRACJAN WOŹNIAK[1], KAROLINA BIELIŃSKA[2], JĘDRZEJ M. JAŚKOWSKI[3]

[1]Veterinary Clinic of Krzysztof Janczewski, DVM, 29 Stycznia 107, 89-422 Sypniewo
[2]Students Buiatric Associatios "Res Ruminantiae", Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University, Szosa Bydgoska 13, 87-100 Torun, Poland
[3]Department of Clinical Sciences and Diagnostic, Institute of Veterinary Medicine, Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University, Szosa Bydgoska 13, 87-100 Toruń, Poland

Received 02.06.2025 *Accepted 15.08.2025*

Kaźmierczak P., Woźniak G., Bielińska K., Jaśkowski J. M.

Digital dermatitis in cattle: Emphasis on non-antibiotic treatment methods

Summary

Digital dermatitis (DD), also known as Mortellaro's disease, is a dermatological condition affecting the bovine digit, characterized by painful inflammatory lesions that result in substantial economic losses in the dairy industry. Despite extensive research, effective treatment and long-term prevention of DD remain challenging. Standard therapeutic approaches include claw trimming, lesion debridement topical or systemic antibiotics, and prophylactic disinfectant footbaths. Recent studies suggest that several non-antibiotic treatment methods show promising therapeutic potential. The efficacy of salicylic acid (SA) and a gel containing chelated copper and zinc (IHF) has been found to be comparable to antibiotics such as tetracycline. Allyl isothiocyanate (AITC) demonstrates antibacterial activity similar to lincomycin, though it may increase pain perception. Other agents, including sodium alginate (ALG) and honey, support lesion healing of DD lesions, though their effectiveness as standalone treatments appears limited. The adoption of alternative therapies aligns with the "One Health" approach and contributes to reducing antibiotic use in cattle farming. While treatments involving SA, IHF, and AITC appear promising, further research is required to confirm their efficacy and to develop long-term therapeutic strategies.

Keywords: digital dermatitis, cattle, non-antibiotic treatments, One Health, dairy farming

Digital dermatitis (DD) is an inflammatory condition of the bovine digital skin, first described in 1974 in Italy by Cheli and Mortellaro (18). Today, the disease is referred to by various names, including Mortellaro's disease, hairy heel warts, strawberry foot, digital warts, and interdigital papillomatosis (92). Similar pathological entities had previously been reported by Wyssmann in 1931, who described the condition as "malignant infectious ulcer of the heel bulb" or "ulcer of the fetlock and hoof" – terms that later evolved into "hoof erosion" or "heel horn erosion" (22). DD lesions typically develop on the plantar skin, proximally to the heel bulb, or within the interdigital space of the bovine claw (5). Clinically, the disease presents as painful, ulcerative, inflammatory lesions that may be acute or chronic and vary in severity (104). Despite decades of research and observation, the etiology and pathogenesis of Mortellaro's disease remain poorly understood. This lack of clarity hampers the establishment of effective treatment protocols and preventive measures (96). Another significant challenge is the early identification of DD lesions, which are often detected only after the onset of lameness or during routine hoof trimming. Healthy limbs and hooves are essential indicators of animal welfare in cattle (37), and DD severely compromises this by causing pain, discomfort, and lameness. As a result, the disease contributes to substantial economic losses, including reduced milk yield, impaired reproductive performance, declining overall health, and increased culling rates (61, 68, 85, 98). The average cost of a single case of DD has been estimated at $133, with only about half of this amount attributed to direct treatment costs (17). Guatteo has reported even higher costs estimating the expense per case at $391.8 (31). In recent years, DD has become a widespread concern in dairy cattle herds globally (16). Therefore, further research and the development of innovative treatment and prevention strategies are of critical importance.

Prevalence

Over the years, numerous studies have identified a wide range of risk factors associated with the occurrence of digital dermatitis (DD). Animal-related predispositions include breed, genetics, individual immune response, parity, and stage of lactation. Environmental factors encompass housing systems, flooring, hoof hygiene and trimming, nutrition, and the introduction of new animals into the herd.

The Holstein-Friesian breed, the primary breed used in dairy farming, is more susceptible to DD than other dairy cattle breeds (8, 38). This increased susceptibility is partly attributed to the conformation of their hooves, specifically, the more acute angle of the hoof walls in Holstein-Friesians. As a result, the heels tend to sink lower, leading to increased contact with manure (8, 29).

One of the most significant risk factors is the housing system. It is well established that keeping cows on concrete or slatted floors negatively impacts hoof horn quality. In contrast, access to pasture or straw-bedded housing significantly reduces both the risk and severity of DD (51, 67, 75, 88, 102). Conversely, DD is more prevalent in barns equipped with robotic milking systems. Tethered cows generally present a lower risk of DD and tend to have cleaner hind limbs compared to those housed in free-stall systems (2, 68, 101). Longer and wider cubicles provide greater comfort, encouraging longer lying times and reduced standing, which limits hoof contact with manure. Infrequent manure removal contributes to hoof horn softening and serves as a reservoir for pathogenic microorganisms, facilitating the spread of infection (29, 50, 51, 88). According to research by de Jong et al., scraping manure at hourly intervals significantly reduces the risk of DD within a herd (41).

Management practices also play a critical role, in the occurrence of digital dermatitis (DD), particularly regarding the timing of regrouping and the introduction of heifers and primiparous cows. Allowing these animals sufficient time to adapt to new environmental conditions is essential (75, 88). The risk of developing DD tends to decrease with each lactation after the second calving; however, this trend may be partially influenced by the culling of cows exhibiting lesions (29, 79). Increased susceptibility to infection is observed during the peak lactation, when the immune system is still weakened postpartum (40). Moreover, during the peak and mid-lactation phases, high-energy diets often result in looser feces, which contribute to greater hoof soiling and elevated DD risk (41, 38, 88). A seasonal pattern in DD incidence has also been documented: cows calving during winter months are more frequently affected compared to those calving in other seasons. Additionally, animals with extended lactation periods exceeding 305 days have demonstrated increased

Tab. 1. Global prevalence of digital dermatitis (DD)

Country	Sample Size (Cows [Herds])	Cow-Level Prevalence (%)	Percentage of Affected Herds (%)	Herd-Level Prevalence (%)
Chile (79)	3,265 (22)	370 (11.3%)	91%	0-40%
Malaysia (81)	251 (8)	16 (8.3%)	–	–
New Zealand (106)	59,849 (127)	649 (1.1%)	49.6%	59.2%
Australia (34)	823	245 (29.8%)	–	–
Canada (86, 41)	3,585 (17)	68%	–	16-81%
	28,607 (156)	20.5%	96.1%	0-74.3%
USA (102)		11.9% of cows 4.2% of heifers	43.5%	–
France (78)	1,782 (40)	38% of primiparous cows 41% of multiparous cows	–	–
Austria (47)	7,765 (512)	33.2%	–	–
Switzerland (29)	24,911 (702)	5.4%	–	36.3%
Netherlands (38, 57)	22,454 (383)	22,454 (21.2%)	–	0-83%
	40,536 (572)	22%	–	–
Norway (84)	2,665 (112)	4.2% (tie-stall housing) 5.7% (free-stall housing)	–	–
Denmark (66, 15)	8,269 (39)	1,993 (24,1%)	97.4%	0-56.2%
	705,803 (1635)	19-22%	90%	–
Ireland (87, 13)	1,204 (10)	5-67.5%*	80%	–
	1,572 (172)[1]	12.4% (grazing season) 13.2% (housing season)	35%	10.1% (grazing season) 9.5% (housing season)
Finland (72)	7,010 (81)	2,195 (31.3%)	91.3%	–
Poland (64)	220 (1)	34 (16%)	–	–

Explanations: [1]Only lame cows were included in the study; *Dependent on the presence of DD alone or in combination with other diseases susceptibility to DD (41). Farms that replenish their herds by purchasing heifers from external sources are approximately three times more likely to experience DD outbreaks compared to farms using home-reared replacements (89). In such cases, implementing proper quarantine protocols is crucial to prevent disease introduction and spread.

Regular hoof trimming is a critical component in maintaining hoof health. Performing hoof trimming at least twice a year facilitates the detection of lesions and reduces the overall number of affected cows (29). However, more frequent trimming – three or more times per year – may paradoxically increase the incidence of DD, as the infectious nature of the disease allows for potential transmission via trimming equipment (2). Nonetheless, the advantages of early detection and prompt treatment generally outweigh the risks associated with less frequent trimming. Moreover, the risk of *Treponema* spp. transmission through trimming tools can be effectively mitigated by implementing proper disinfection protocols (7, 80).

Assessment of DD Severity

DD lesions are classified using the M-system scoring. This system includes the following categories: M0 – normal claw skin without any signs of DD; M1 – early-stage lesions, small and limited in size (less than 2 cm in diameter), typically red to grey in color; M2 – acute ulcerative lesions larger than 2 cm in diameter, red or red-grey in appearance; M3 – healing stage, characterized by hard, scab-like tissue covering previously active DD lesions; M4 – chronic stage presenting hyper keratotic and/or proliferative tissue changes; M4.1 – a chronic lesion exhibiting features of both M4 and M1 stages (25).

Treatment

Lameness in cattle is typically managed through corrective hoof trimming, thorough cleaning of lesions, and, when indicated, the local or systemic administration of antibiotics. In cases of DD, a commonly used treatment protocol includes debridement of the affected areas followed by the topical application of oxytetracycline or lincomycin under a gauze dressing and bandage (6, 11, 73). Although systemic antibiotic administration has also been reported, its use is limited due to concerns related to withdrawal periods. In herds with a high risk of DD or in which the disease is already present, the use of prophylactic hoof baths containing disinfectant and bactericidal agents is recommended as part of routine herd management (53, 54).

Salicylic acid (SA)

Salicylic acid (2-hydroxybenzoic acid, SA) is widely known for its keratolytic, anti-inflammatory, and disinfectant properties. Commercially available pastes and powders containing SA are formulated for treating skin conditions in the interdigital area of cattle, primarily *digital dermatitis* (DD) and interdigital phlegmon (14, 70, 82). Methyl salicylate, a component of these preparations, stimulates circulation and phagocytosis and helps dissolves the intercellular cement in the stratum corneum (9). Its antibacterial effect is attributed to the inhibition of bacterial replication mechanisms (49).

Studies assessing the effectiveness of SA in treating DD (4, 14, 45, 82, 101) typically involve applying the paste or powder to a previously cleaned lesion, including a margin of surrounding healthy tissue. The area is then covered with gauze and a bandage. The healing process is evaluated after several days to a few weeks, and the procedure is repeated as needed until full recovery is achieved. Clinical improvement is usually observed within 2 to 5 weeks, although some cows may experience relapse (4, 14, 45, 82, 101). The reported effectiveness of this treatment varies and appears to depend on the treatment protocol, specific formulation, environmental conditions, and the stage of the disease. The highest treatment success rates are observed in M2-stage lesions, which tend to heal more easily to M0, with improvement noted as early as 3 days post-treatment (4, 82). Repeated applications are often effective for chronic or poorly healing lesions.

Tab. 2. Effectiveness of current DD treatment methods

Active substance	Reported Effectiveness	Achieved Degree of Improvement	Time to Improvement/Healing
Oxytetracycline (spray) (39)	75%	M4/M0*	28 days
Tetracycline hydrochloride (2-5 g powder) (21)	57%	Cured	8-12 days
Thiamphenicol (spray) (39)	89%	M4/M0*	28 days
Lincomycin (10 g powder) (11)	68%	Cured	30 days
Erythromycin (35 mg/l hoof bath) (54)	60%	Improvement	4 days
Copper sulfate (7.5% hoof bath) (28)	88%	Prevention	–
Procaine penicillin (18,000 IU/kg IM × 6) (75)	100%	Cured	–
Ceftiofur (2 mg/kg IM × 3) (75)	87%	Cured	–
Cefquinome (1 mg/kg IM × 3 or × 5) (52)	Improved results after a 5-day therapy	–	–
Erythromycin (10 mg/kg IM once) (52)	Comparable to erythromycin footbaths	–	–

Explanations: * M0 – normal claw skin without any signs of DD; M4 – late-stage, chronic lesions characterized by hyperkeratotic and/or proliferative tissue changes

Proliferative lesions, classified as M4, are more difficult to treat and may require prolonged SA exposure to penetrate deeper skin layers, where *Treponema* spp. can persist in a protected form, contributing to recurrence (24, 44). The proportion of cows with M4 lesions achieving permanent recovery ranged from 13.6%, while success rates for M2 lesions reached up to 100%. Overall, treatment with SA resulted in improvement rates exceeding 36.9% (4, 14, 45, 82, 101).

In one study, histopathological results of biopsy samples from areas previously treated with salicylic acid revealed no inflammatory changes or only mild to moderate perivascular, chronic lymphoplasmacytic dermatitis, without evidence of ulceration or abnormal keratinization. Additionally, RT-PCR testing detected no spirochetal DNA in 88% of the samples (4). In another study, modified Warthin-Starry staining revealed the absence of spirochetes in 43% of samples from DD-affected areas post-SA treatment, while 36% of samples contained only small amounts of spirochetes limited to the epidermis. Overall, 63% of healed lesions were free of spirochetes (14). Comparative studies evaluating the effectiveness of tetracyclines versus salicylic acid in the treatment of DD demonstrated that SA was more effective than tetracycline spray. After 21 days of treatment, the cure rate with SA was 1.75 times higher than with tetracyclines (45). In another study, after 34 days, the cure rate was 2.3 to 2.75 times higher with SA (82). These studies, however, assessed only short-term clinical improvement and did not provide information on potential relapse rates.

SA also exhibits anti-inflammatory properties, which help to alleviate inflammation and reduce pain associated with DD (82). Its use is particularly indicated for hyperkeratotic and dyskeratotic lesions; however, application to ulcerated areas may cause discomfort and the potential for local irritation (94). A limitation of this treatment approach is the requirement for a dressing after each application, necessitating limb lifting and animal restraint during every procedure. Comparable therapeutic outcomes in DD treatment have been reported with the use of other preparations containing inorganic or organic acids (14, 46).

Chelated copper and zinc (IHF)

Copper plays a significant role in wound healing due to its potential biocidal properties and its function as a cofactor in the synthesis and stabilization of extracellular matrix proteins in the skin. It also promotes angiogenesis, thereby supporting tissue regeneration (12). Zinc, likewise, is an essential cofactor for numerous metalloenzymes involved in membrane repair, cellular proliferation, and immune function. Zinc deficiency has been associated with impaired wound healing and the development of dermatological lesions (56). The chelation of these metals results in the formation of organic complexes that enhance tissue absorption and bioavailability (32).

The treatment of DD in cattle with a gel containing chelated copper and zinc typically involves application to previously trimmed and cleaned hooves at the site of lesions. Following application, dressings are applied, and the healing process is assessed at specific intervals: on days 7, 14, 21, and 28 (35); on days 3, 7, and 10 (95); or weekly over a five-week period (43). Reported treatment efficacy within 7 to 10 days ranged from 86.8% to 100%, with all M2-stage lesions showing clinical improvement (23, 35, 95). In the study by Holzhauer's et al. (35), complete healing (transition to M0) was achieved in 50% of cows after 28 days. In contrast, another study reported that only 4% of lesions reached M0 after 10 days of treatment (95). Despite this variation, the overall healing rate in both studies ranged from 92% to 94%, although lesions classified as M4 – representing the chronic non-painful stage of DD – were also included among the healed cases (35, 95). Only one study evaluated the long-term efficacy of IHF treatment. It reported a healing rate of 33.3%, after one week, increasing to 71% after five weeks (43).

Studies comparing the effectiveness of the IFH gel with the commonly used topical chlortetracycline have yielded variable results. One study reported that, after 28 days, the proportion of completely healed lesions was 92% for IHF and 58% for chlortetracycline – a difference of 34 percentage points (35). In contrast, another study found that after 28 days, the healing rates were 81.8% for chlortetracycline and 63.2% for IHF, increasing to 86% and 71%, respectively, after 35 days (43).

None of the available studies assessed histological or cytological changes during treatment. The effectiveness of IHF was evaluated solely based on clinical examination and organoleptic assessment, which introduces a degree of subjectivity. Moreover, the limited number of studies and absence of long-term follow-up hinder definitive conclusions regarding the efficacy of IHF. Interpretation of clinical healing may also be confounded by the pharmacological action of IHF components. Copper, for instance, acts as an astringent and drying agent, that promotes healing – specifically, the transition to the M3 stage, characterized by scab formation. This effect may obscure accurate lesion evaluation (25).

There are limited reports on the prophylactic and therapeutic use of IHF in the form of hoof baths or sprays (19, 76, 77). The reported effectiveness varies widely, ranging from 38% to 98%, depending on the specific treatment protocol employed (19, 76, 77). However, the broad application of IHF – particularly in hoof baths – raises environmental concerns due to its potential toxicity.

Allyl isothiocyanate (AITC)

Recent years have seen growing interest in the use of plant-derived extracts. One such compound is allyl isothiocyanate (AITC), which is obtained from plants of the *Brassicaceae* family, including Japanese horseradish (*Wasabia japonica*) and mustard greens (*Brassica juncea*) (90). AITC demonstrates strong antibacterial activity against Gram-negative bacteria, such as *Salmonella* Montevideo (55) and *Escherichia coli* O157:H7 (55, 59), as well as Gram-positive bacteria, including *Staphylococcus aureus* (58). Its antibacterial effect primarily results from the inhibition of bacterial macromolecule biosynthesis during the growth phase (36).

Current research indicates that AITC alleviates digital dermatitis (DD) lesions within two days of treatment, reducing lesion severity from stage M2 to M4, M3, or M1 (20, 105). Microscopic examination following a two-day course of AITC combined with hoof trimming revealed an absence of *Treponema*-like spirochetes on the lesion surface, and histopathological analysis showed no presence of these spirochetes within the keratin layer by day six (105). Overall, no significant difference in therapeutic efficacy was observed between AITC and lincomycin treatments. Analysis of the 16S rRNA amplicon from DD microbiota identified operational taxonomic units (OTUs) assigned to the genus *Treponema* in less than 5% of the population following both therapies. Notably, some individuals did not respond to either treatment modality (20, 30).

Importantly, AITC administration may transiently increase perceived pain due to the binding of plant-derived compounds to TRPA1 cation channels, leading to the activation of nociceptors and the induction of an inflammatory response (42, 97).

Sodium alginate (ALG)

Sodium alginate (ALG) has gained popularity in veterinary medicine due to its efficacy in treating udder cleft dermatitis (UCD) in dairy cows (103). Derived from the cell walls of brown algae, ALG exhibits significant wound-healing potential owing to its gel-forming properties, which mimic the structure of the extracellular matrix (1). Commercially available ALG gels also contain the enzymatic system GLG (glucose oxidase, lactoperoxidase, and guaiacol), which facilitates the controlled release of free radicals that selectively target and destroy bacterial cell walls (83).

Studies evaluating the effectiveness of ALG in the treatment of digital dermatitis (DD) have not produced results comparable to those observed in the treatment of UCD. Chiba et al. reported that a two-day course of ALG applied under a bandage to M2-stage lesions resulted in no clinical improvement (20). Similar conclusions were reached by Hesseling, Vanhoudt, and colleagues, who observed clinical improvement in only 27-29% of lesions after 10 days, with complete healing achieved in just 0-2% of cases (33, 95). Although Hesseling attributed these poor outcomes to the short observation period, subsequent studies reported no improvement up to week 11 and documented a high relapse risk (0.55). In contrast, treatment with metal chelates comparable lesion stages resulted in 84-92.5% clinical improvement and a lower relapse risk of 0.29 (20, 95).

Based on these findings, sodium alginate does not appear to be a viable alternative as a monotherapy for DD when compared to currently established treatment methods.

Honey

The therapeutic use of honey dates back to approximately 2000 BCE, when it was applied topically for the treatment of wounds and burns (63). While honey is widely used in human medicine globally, application in veterinary medicine has garnered increasing interest since 2010 (60, 71). Honey exhibits antibacterial, antiproliferative, anti-inflammatory, and antimutagenic properties (3, 62). Although it is primarily composed of sugars, honey also contains numerous vitamins, minerals, antioxidants, and enzymes (27).

To date, only a limited number of studies have investigated the interventional use of honey in the treatment of digital dermatitis (DD) in cattle. One study involving over 130 DD-affected hooves utilized cornflower honey, which is noted for its higher average hydrogen peroxide production – an important factor in its antibacterial activity – as well as its ability to enhance blood flow and stimulate the healing process compared to other honey types (26, 93). The treatment protocol included weekly hoof trimming and cleaning, followed by the application of 10 g of cornflower honey to the lesion, and subsequent bandaging. After two weeks, the probability of healing increased to 40% for chronic lesions and 55% for early-stage lesions, compared to control groups that received only cleaning and trimming (8%) or cleaning, trimming, and bandaging (30%). After four weeks, more than 80% of all hooves treated with cornflower honey had formed a complete epithelial layer and were considered healed (65).

Two subsequent studies evaluated the efficacy of honey as part of a combination therapy. The treatment protocol involved a single application of a honey-iodine paste to DD lesions under a bandage, combined with hoof baths in an acidified 5% copper sulfate solution twice weekly. This regimen resulted in a 25% healing rate (M0 stage) after three days. However, the proportion of healed lesions declined over time, suggesting recurrence of the disease, and average lesion size increased. By day 28, M1 and M2 lesions had progressed to M4.1, and only 11% of lesions remained at M0. The overall healing efficacy at day 120 was estimated at 44.4% when both M0 and M4 stages were considered. Compared to treatment using a copper sulfate-iodine paste under a bandage alone, the odds ratio for healing in this combined approach was more than four times higher (69).

Currently, a commercially available paste containing honey, salicylic acid, and glycerol is marketed in

Europe. A study assessing its efficacy involved 19 cows with DD lesions classified as stages M2 and M4.1. Following hoof trimming, the paste was applied to the lesions and covered with a bandage. Treatment progress was evaluated on days 3, 7, 10, and 14, with repeated application as needed. By day 14, 95% of lesions were considered healed. However, this included lesions at stages M3 (40%), M4 (47.5%), and M0 (7.5%), with only stage M0 representing complete healing. A limitation of this study was the concurrent evaluation of both the honey paste and IHF paste on lesions of the same stage, with results reflecting the combined efficacy of both treatments (91).

Given the limited number of studies on the efficacy of honey as monotherapy for DD and the variability in reported outcomes, definitive conclusions cannot be drawn. Further randomized controlled trials are warranted, incorporating control groups, differentiating by honey type, and including diagnostic assessments for the presence of *Treponema* species.

New directions in the treatment of digital dermatitis

Cholecalciferol (vitamin D_3). Cholecalciferol does not have a direct antibacterial or anti-inflammatory effect on digital dermatitis lesions, but it stimulates the production of natural skin defense peptides, such as β-defensins. It can act as an adjunct in DD therapy by increasing local skin immunity. However, studies to date have not confirmed its effectiveness as a stand-alone treatment in clinical settings (100).

Silver nanoparticles. *In vitro* studies have shown that silver nanoparticles have a strong bactericidal effect on pathogens responsible for DD. They may be a potential alternative or supplement to traditional methods, but there is a lack of research confirming their effectiveness in farm conditions and in dairy cattle populations (48).

Calcium hydroxide. When used in hoof baths, it has been shown to reduce the number of active DD lesions and prevent recurrence. Its action is based on a strongly alkaline reaction that inhibits bacterial growth. However, the risk of local skin burns resulting from the high pH of the preparation should be taken into account (74).

The three therapeutic approaches described – namely, cholecalciferol supplementation, the use of silver nanoparticles, and the use of calcium hydroxide in hoof baths – are based on the results of single, preliminary studies. The mechanisms of action presented are of interest, and there is considerable practical potential, but it is essential that these results are interpreted with great caution. In order to reach a conclusion, it is necessary to conduct further extensive and well-planned field studies on larger cattle populations.

In the „One Health" approach, efforts are being made to minimize the use of antibiotics in cattle production. Alternative methods for treating digital dermatitis (DD) are a rapidly evolving area of research. Currently, commercially available products combining the aforementioned active substances have demonstrated promising efficacy. Further studies are necessary to validate their long-term effectiveness under different farming conditions, assess potential resistance development, and evaluate their economic feasibility. A continued focus on integrated herd management, early detection, and preventative strategies will be essential to sustainably control DD while aligning with global antimicrobial stewardship goals.

References

1. *Abourehab M. A. S., Rajendran R. R., Singh A., Pramanik S., Shrivastav P., Ansari M. J., Manne R., Amaral L. S., Deepak A.*: Alginate as a promising biopolymer in drug delivery and wound healing: A review of the State-of-the-Art. Int. J. Mol. Sci. 2022, 23, 9035.
2. *Ahlén L., Holmøy I. H., Nødtvedt A., Sogstad Å. M., Fjeldaas T.*: A case-control study regarding factors associated with digital dermatitis in Norwegian dairy herds. Acta Vet. Scand. 2022, 64.
3. *Ahmed S., Othman N. H.*: Honey as a potential natural anticancer agent: A review of its mechanisms. Evidence-based Complementary and Alternative Medicine 2013.
4. *Alsaaod M., Jensen T. K., Miglinci L., Gurtner C., Brandt S., Plüss J., Studer E., Steiner A.*: Proof of an optimized salicylic acid paste-based treatment concept of ulcerative M2-stage digital dermatitis lesions in 21 dairy cows. PLoS One 2022, 17.
5. *Alsaaod M., Locher I., Jores J., Grimm P., Brodard I., Steiner A., Kuhnert P.*: Detection of specific Treponema species and Dichelobacter nodosus from digital dermatitis (Mortellaro's disease) lesions in Swiss cattle. Schweiz. Arch. Tierheilkd. 2019, 161, 207-215.
6. *Apley M. D.*: Clinical evidence for individual animal therapy for papillomatous digital dermatitis (hairy heel wart) and infectious bovine pododermatitis (foot rot). Veterinary Clinics of North America – Food Animal Practice 2015, 31, 81-95.
7. *Bayer M., Strauss G., Syring C., Ruiters M., Becker J., Steiner A.*: Implementation of biosecurity measures by hoof trimmers in Switzerland. Schweiz. Arch. Tierheilkd. 2023, 165, 307-320.
8. *Becker J., Steiner A., Kohler S., Koller-Bähler A., Wüthrich M., Reist M.*: Lahmheit und Klauenerkrankungen bei Schweizer Milchkühen: II. Risikofaktoren. Schweiz. Arch. Tierheilkd. 2014, 156, 79-89.
9. *Behnam S., Villarama I., Dreher F., Maibach H. I.*: The keratolytic effects of short term salicylic acid on the stratum corneum. J. Am. Acad. Dermatol. 2005, 52, 78-78.
10. *Belyakova N., Kovalenko A., Bodrova Y.*: Development of drugs for treatment of Mortellaro's Disease in cattle, [in:] 1st International Symposium Innovations in Life Sciences (ISILS 2019). Atlantis Press 2019, 128-134.
11. *Berry S. L., Read D. H., Walker R. L., Famula T. R.*: Clinical, histologic, and bacteriologic findings in dairy cows with digital dermatitis (footwarts) one month after topical treatment with lincomycin hydrochloride or oxytetracycline hydrochloride. J. Am. Vet. Med. Assoc. 2010, 237, 555-560.
12. *Borkow G.*: Using copper to improve the well-being of the skin. Curr. Chem. Biol. 2014, 8, 89.
13. *Browne N., Hudson C. D., Crossley R. E., Sugrue K., Huxley J. N., Conneely M.*: Hoof lesions in partly housed pasture-based dairy cows. J. Dairy Sci. 2022, 105, 9038-9053.
14. *Capion N., Larsson E. K., Nielsen O. L.*: A clinical and histopathological comparison of the effectiveness of salicylic acid to a compound of inorganic acids for the treatment of digital dermatitis in cattle. J. Dairy Sci. 2018, 101, 1325-1333.
15. *Capion N., Raundal P., Foldager L., Thomsen P. T.*: Status of claw recordings and claw health in Danish dairy cattle from 2013 to 2017. Veterinary Journal 2021, 277.
16. *Capion N., Thamsborg S. M., Enevoldsen C.*: Prevalence of foot lesions in Danish Holstein cows. Vet. Rec. 2008, 163, 80-86.
17. *Cha E., Hertl J. A., Bar D., Gröhn Y. T.*: The cost of different types of lameness in dairy cows calculated by dynamic programming. Prev. Vet. Med. 2010, 97, 1-8.
18. *Cheli R., Morterello C.*: The 8th International Conference on Diseases of Cattle, [in:] La Dermatite Digitale Del Bovino. Piacenza, Milan, Italy 1994, 208-213.
19. *Chen Y. H., Chen Y. M., Tu P. A., Yeh Y. H., Lee K. H., Hsu J. T.*: Efficacy of quaternary ammonium salt-based disinfectant or chelated copper–zinc footbath solution in the treatment of digital dermatitis on one research dairy farm in Taiwan. Vet. Dermatol. 2023, 34, 608-617.

20. *Chiba K., Miyazaki T., Sekiyama Y., Miyazaki M., Okada K.*: The therapeutic efficacy of allyl isothiocyanate in cows with bovine digital dermatitis. Journal of Veterinary Medical Science 2017, 79, 1191-1195.
21. *Cutler J. H. H., Cramer G., Walter J. J., Millman S. T., Kelton D. F.*: Randomized clinical trial of tetracycline hydrochloride bandage and paste treatments for resolution of lesions and pain associated with digital dermatitis in dairy cattle. J. Dairy Sci. 2013, 96, 7550-7557.
22. *Dirksen G., Grunder H.-D., Stober M.*: Choroby wewnętrzne i chirurgia bydła 2015 III. ed.
23. *Dotinga A., Jorritsma R., Nielen M., Phd D., Ecvph D.*: A randomised non-inferiority trial on the effect of an antibiotic or non-antibiotic topical treatment protocol for digital dermatitis in dairy cattle. Veterinary Evidence 2017, 2.
24. *Döpfer D., Anklam K., Mikheil D., Ladell P.*: Growth curves and morphology of three Treponema subtypes isolated from digital dermatitis in cattle. The Veterinary Journal 2012, 193, 685-693.
25. *Döpfer D., Koopmans A., Meijer F. A., Szakáll I., Schukken Y. H., Klee W., Bosma R. B., Cornelisse J. L., Asten A. J. A. M. van, Huurne A. A. H. M. ter.*: Histological and bacteriological evaluation of digital dermatitis in cattle, with special reference to spirochaetes and Campylobacter faecalis. Vet. Rec. 1997, 140, 620-623.
26. *Dustmann J. H.*: Antibacterial effect of honey. Apiacta 1979, 1.
27. *Eteraf-Oskouei T., Najafi M.*: Traditional and modern uses of natural honey in human diseases: A review. Iran J. Basic Med. Sci. 2013, 16, 731.
28. *Fjeldaas T., Knappe-Poindecker M., Bøe K. E., Larssen R. B.*: Water footbath, automatic flushing, and disinfection to improve the health of bovine feet. J. Dairy Sci. 2014, 97, 2835-2846.
29. *Fürmann A., Syring C., Becker J., Sarbach A., Weber J., Welham Ruiters M., Steiner A.*: Prevalence of painful lesions of the digits and risk factors associated with digital dermatitis, ulcers and white line disease on Swiss cattle farms. Animals 2024, 14, 153.
30. *Gotoh Y., Chiba K., Sekiyama Y., Okada K., Hayashi T., Misawa N.*: 16S rRNA-based amplicon analysis of changes in the bacterial population in the lesions of papillomatous digital dermatitis in dairy cattle after topical treatment with allyl isothiocyanate. Microbiol. Immunol. 2020, 64, 416-423.
31. *Guatteo R.*: Control of digital dermatitis in cattle an evidence based approach. 32 World Buiatric Congress, 20-24 Mai, Cancun 2024, 84-90.
32. *Guo H., Yu Y., Hong Z., Zhang Y., Xie Q., Chen H.*: Effect of collagen peptide-chelated zinc nanoparticles from pufferfish skin on zinc bioavailability in rats. Journal of Medicinal Food 2021, 24 (9), 987-996.
33. *Hesseling J.*: The efficacy of a non-antibiotic enzyme alginogel on digital dermatitis in dairy cattle. 2019.
34. *Hesseling J., Legione A. R., Stevenson M. A., McCowan C. I., Pyman M. F., Finochio C., Nguyen D., Roic C. L., Thiris O. L., Zhang A. J., van Schaik G., Coombe J. E.*: Bovine digital dermatitis in Victoria, Australia. Aust. Vet. J. 2019, 97, 404-413.
35. *Holzhauer M., Bartels C. J., Van Barneveld M., Vulders C., Lam T.*: Curative effect of topical treatment of digital dermatitis with a gel containing activated copper and zinc chelate. Veterinary Record 2011, 169, 555.
36. *Holzhauer M., Bartels C. J. M., Döpfer D., van Schaik G.*: Clinical course of digital dermatitis lesions in an endemically infected herd without preventive herd strategies. The Veterinary Journal 2008, 177, 222-230.
37. *Holzhauer M., Bartels C. J. M., van den Borne B. H. P., van Schaik G.*: Intra-class correlation attributable to claw trimmers scoring common hind-claw disorders in Dutch dairy herds. Prev. Vet. Med. 2006, 75, 47-55.
38. *Holzhauer M., Hardenberg C., Bartels C. J. M., Frankena K.*: Herd- and cow-level prevalence of digital dermatitis in The Netherlands and associated risk factors. J. Dairy Sci. 2006, 89, 580-588.
39. *Holzhauer M., Ploegmakers-Van Deventer R., Smits D., Swart W.*: Comparing the curative efficacy of topical treatment with thiamphenicol and oxytetracycline on digital dermatitis lesions in dairy cattle. Vet. Rec. 2017, 180, 500.
40. *Jesús Argáez-Rodríguez F. de, Hird D. W., Hernández De Anda J., Read D. H., Rodríguez-Lainz A.*: Papillomatous digital dermatitis on a commercial dairy farm in Mexicali, Mexico: Incidence and effect on reproduction and milk production. Prev. Vet. Med. 1997, 32, 275-286.
41. *Jong E. de, Frankena K., Orsel K.*: Risk factors for digital dermatitis in free-stall-housed, Canadian dairy cattle. Vet. Rec. Open 2021, 8.
42. *Jordt S. E., Bautista D. M., Chuang H. H., McKemy D. D., Zygmunt P. M., Högestätt E. D., Meng I. D., Julius D.*: Mustard oils and cannabinoids excite sensory nerve fibres through the TRP channel ANKTM1. Nature 2004, 427, 6971, 260-265.
43. *Klawitter M., Döpfer D., Braden T. B., Amene E., Mueller K. E.*: Randomised clinical trial showing the curative effect of bandaging on M2-stage lesions of digital dermatitis in dairy cows. Vet. Rec. Open 2019, 6.
44. *Klitgaard K., Boye M., Capion N., Jensen T. K.*: Evidence of multiple Treponema phylotypes involved in bovine digital dermatitis as shown by 16S rRNA gene analysis and fluorescence in situ hybridization. J. Clin. Microbiol. 2008, 46, 3012-3020.
45. *Kofler J., Innerebner C., Pesenhofer R., Hangl A., Tichy A.*: Effectiveness of salicylic acid paste for treatment of digital dermatitis in dairy cows compared with tetracycline spray and hydrotherapy. Berl. Munch. Tierarztl. Wochenschr. 2015, 128, 326-334.
46. *Kofler J., Pospichal M., Hofmann-Parisot M.*: Efficacy of the non-antibiotic paste Protexin® Hoof-Care for topical treatment of digital dermatitis in dairy cows. Journal of Veterinary Medicine Series A: Physiology Pathology Clinical Medicine 2004, 51, 447-452.
47. *Kofler J., Suntinger M., Mayerhofer M., Linke K., Maurer L., Hund A., Fiedler A., Duda J., Egger-Danner C.*: Benchmarking based on regularly recorded claw health data of Austrian dairy cattle for implementation in the cattle data network (RDV). Animals 2022, 12, 808.
48. *Kot M., Kalińska A., Jaworski S., Wierzbicki M., Smulski S., Gołębiewski M.*: In vitro studies of nanoparticles as a potentially new antimicrobial agent for the prevention and treatment of lameness and digital dermatitis in cattle. Int. J. Mol. Sci. 2023, 24 (7), 6146.
49. *Kupferwasser L. I., Yeaman M. R., Nast C. C., Kupferwasser D., Xiong Y.-Q., Palma M., Cheung A. L., Bayer A. S.*: Salicylic acid attenuates virulence in endovascular infections by targeting global regulatory pathways in Staphylococcus aureus. Journal of Clinical Investigation 2003, 112, 222-233.
50. *Laven R.*: Determination of the factors affecting the cause, prevalence and severity of digital dermatitis as a major cause of lameness in dairy cows. Cirencester 2000.
51. *Laven R.*: The environment and digital dermatitis. Cattle Practice 1999, 7, 349-354.
52. *Laven R. A.*: Efficacy of systemic cefquinome and erythromycin against digital dermatitis in cattle. Veterinary Record 2006, 159, 19-20.
53. *Laven R. A., Logue D. N.*: Treatment strategies for digital dermatitis for the UK. Vet. J. 2006, 171, 79-88.
54. *Laven R. A., Proven M. J.*: Use of an antibiotic footbath in the treatment of bovine digital dermatitis. Veterinary Record 2000, 147, 503-506.
55. *Lin C. M., Preston J. F., Wei C. I.*: Antibacterial mechanism of allyl isothiocyanate. J. Food Prot. 2000, 63, 727-734.
56. *Lin P. H., Sermersheim M., Li H., Lee P. H. U., Steinberg S. M., Ma J.*: Zinc in Wound Healing Modulation. Nutrients 2018, 10.
57. *Linde C. van der, de Jong G., Koenen E. P. C., Eding H.*: Claw health index for Dutch dairy cattle based on claw trimming and conformation data. J. Dairy Sci. 2010, 93, 4883-4891.
58. *Lu Z., Dockery C. R., Crosby M., Chavarria K., Patterson B., Giedd M.*: Antibacterial activities of wasabi against Escherichia coli O157:H7 and Staphylococcus aureus. Front Microbiol. 2016, 7.
59. *Luciano F. B., Holley R. A.*: Enzymatic inhibition by allyl isothiocyanate and factors affecting its antimicrobial action against Escherichia coli O157:H7. Int. J. Food Microbiol. 2009, 131, 240-245.
60. *McLoone P., Oluwadun A., Warnock M., Fyfe L.*: Honey: A Therapeutic agent for disorders of the skin. Cent. Asian J. Glob. Health 2016, 5.
61. *Melendez P., Bartolome J., Archbald L. F., Donovan A.*: The association between lameness, ovarian cysts and fertility in lactating dairy cows. Theriogenology 2003, 59, 927-937.
62. *Molan P. C.*: Potential of honey in the treatment of wounds and burns. Am. J. Clin. Dermatol. 2001, 2, 13-19.
63. *Molan P. C.*: The antibacterial activity of honey. Bee World 1992, 73, 5-28.
64. *Nałęcz-Tarwacka T., Jedrzejek D.*: Influence of the selected hoof diseases on reproduction parameters of Polish HF cows. Acta Sci. Pol. Zootechnica 2012, 11, 79-90.
65. *Oelschlaegel S., Pieper L., Staufenbiel R., Gruner M., Zeippert L., Pieper B., Koelling-Speer I., Speer K.*: Floral markers of cornflower (centaurea cyanus) honey and its peroxide antibacterial activity for an alternative treatment of digital dermatitis. J. Agric Food Chem. 2012, 60, 11811-11820.
66. *Oliveira V. H. S., Sørensen J. T., Thomsen P. T.*: Associations between biosecurity practices and bovine digital dermatitis in Danish dairy herds. J. Dairy Sci. 2017, 100, 8398-8408.
67. *Onyiro O. M., Andrews L. J., Brotherstone S.*: Genetic parameters for digital dermatitis and correlations with locomotion, production, fertility traits, and longevity in Holstein-Friesian dairy cows. J. Dairy Sci. 2008, 91, 4037-4046.
68. *Palmer M. A., O'Connell N. E.*: Digital dermatitis in dairy cows: A review of risk factors and potential sources of between-animal variation in susceptibility. Animals 2015, 5, 512-535.
69. *Paudyal S., Manriquez D., Velasquez A., Shearer J. K., Plummer P. J., Melendez P., Callan R. J., Sorge U. S., Bothe H., Velez J., Pinedo P. J.*: Efficacy of non-antibiotic treatment options for digital dermatitis on an organic dairy farm. The Veterinary Journal 2020, 255, 105417.
70. *Persson Y., Mörk M. J., Pringle M., Bergsten C.*: A case-series report on the use of a salicylic acid bandage as a non-antibiotic treatment for early detected, non-complicated interdigital phlegmon in dairy cows. Animals 2019, 9.

71. *Pham M. T., Rajić A., Greig J. D., Sargeant J. M., Papadopoulos A., Mcewen S. A.*: A scoping review of scoping reviews: Advancing the approach and enhancing the consistency. Res. Synth. Methods 2014, 5, 371-385.
72. *Pirkkalainen H., Riihimäki A., Simojoki H., Soveri T., Rajala-Schultz P. J., Hintikka T., Pelkonen S., Kontturi M., Kujala-Wirth M.*: Prevalence of digital dermatitis using mirror scoring in Finnish freestall dairy herds. J. Dairy Sci. 2021, 104, 9173-9184.
73. *Plummer P. J., Krull A.*: Clinical perspectives of digital dermatitis in dairy and beef cattle. Veterinary Clinics of North America – Food Animal Practice 2017, 33, 165-181.
74. *Rasmussen A. S., Bennedsgaard T. W., Capion N.*: Evaluation of calcium hydroxide ($Ca(OH)_2$) used in footbaths as treatment and prevention of digital dermatitis in Danish dairy cattle. J. Dairy Sci. 2012.
75. *Read D. H., Walker R. L.*: Papillomatous digital dermatitis (footwarts) in California dairy cattle: Clinical and gross pathologic findings. Journal of Veterinary Diagnostic Investigation 1998, 10, 67-76.
76. *Relun A., Lehebel A., Bareille N., Guatteo R.*: Effectiveness of different regimens of a collective topical treatment using a solution of copper and zinc chelates in the cure of digital dermatitis in dairy farms under field conditions. J. Dairy Sci. 2012, 95, 3722-3735.
77. *Relun A., Lehebel A., Bruggink M., Bareille N., Guatteo R.*: Estimation of the relative impact of treatment and herd management practices on prevention of digital dermatitis in French dairy herds. Prev. Vet. Med. 2013, 110, 558-562.
78. *Relun A., Lehebel A., Chesnin A., Guatteo R., Bareille N.*: Association between digital dermatitis lesions and test-day milk yield of Holstein cows from 41 French dairy farms. J. Dairy Sci. 2013, 96, 2190-2200.
79. *Rodriguez-Lainz A., Melendez-Retamal P., Hird D. W., Read D. H., Walker R. L.*: Farm- and host-level risk factors for papillomatous digital dermatitis in Chilean dairy cattle. Prev. Vet. Med. 1999, 42, 87-97.
80. *Sadiq M. B., Ramanoon S. Z., Mansor R., Syed-Hussain S. S., Mossadeq W. M. S.*: Claw trimming as a lameness management practice and the association with welfare and production in dairy cows. Animals 2020, 10, 1-18.
81. *Sadiq M. B., Ramanoon S. Z., Mansor R., Syed-Hussain S. S., Mossadeq W. M. S.*: Prevalence of lameness, claw lesions, and associated risk factors in dairy farms in Selangor, Malaysia. Trop. Anim. Health Prod. 2017, 49, 1741.
82. *Schultz N., Capion N.*: Efficacy of salicylic acid for treatment of digital dermatitis in dairy cattle. Vet. J. 2013, 198, 518-523.
83. *Smet K. de, Van Den Plas D., Lens D., Sollie P.*: Pre-clinical evaluation of a new antimicrobial enzyme for the control of wound bioburden. Wounds 2009, 21, 65-73.
84. *Sogstad Å. M., Fjeldaas T., Østerås O., Forshell K. P.*: Prevalence of claw lesions in Norwegian dairy cattle housed in tie stalls and free stalls. Prev. Vet. Med. 2005, 70, 191-209.
85. *Sogstad Å. M., Østerås O., Fjeldaas T., Nafstad O.*: Bovine claw and limb disorders related to culling and carcass characteristics. Livest Sci. 2007, 106, 87-95.
86. *Solano L., Barkema H. W., Jacobs C., Orsel K.*: Validation of the M-stage scoring system for digital dermatitis on dairy cows in the milking parlor. J. Dairy Sci. 2017, 100, 1592-1603.
87. *Somers J., O'Grady L.*: Foot lesions in lame cows on 10 dairy farms in Ireland. Ir. Vet. J. 2015, 68.
88. *Somers J. G. C. J., Frankena K., Noordhuizen-Stassen E. N., Metz J. H. M.*: Risk factors for digital dermatitis in dairy cows kept in cubicle houses in The Netherlands. Prev. Vet. Med. 2005, 71, 11-21.
89. *Sullivan L. E., Carter S. D., Blowey R., Duncan J. S., Grove-White D., Evans N. J.*: Digital dermatitis in beef cattle. Veterinary Record 2013, 173, 582.
90. *Sultana T., Savage G. P., McNeil D. L., Porter N. G., Martin R. J., Deo B.*: Effects of fertilisation on the allyl isothiocyanate profile of above-ground tissues of New Zealand-grown wasabi. J. Sci. Food Agric. 2002, 82, 1477-1482.
91. *Tikka A. M.*: Comparison of two different treatment strategies for bovine digital dermatitis. Estonian University of Life Sciences, Tartu 2023.
92. *Tunç A. S., Çağatay S., Sağlam M., Kutsal O.*: Pathomorphological findings of Mortellaro disease in dairy cattle 2021, 68, 245-250.
93. *Tur E., Bolton L., Constantine B. E.*: Topical hydrogen peroxide treatment of ischemic ulcers in the guinea pig: blood recruitment in multiple skin sites. J. Am. Acad. Dermatol. 1995, 33, 217-221.
94. *Vanhoudt A.*: Diagnosis, treatment, and control of bovine digital dermatitis in dairy cattle. Utrecht University 2023.
95. *Vanhoudt A., Hesseling J., Nielen M., Wilmink J., Jorritsma R., van Werven T.*: M-score and wound healing assessment of 2 nonantibiotic topical gel treatments of active digital dermatitis lesions in dairy cattle. J. Dairy Sci. 2022, 105, 695-709.
96. *Vermeersch A., Opsomer G.*: Digital dermatitis in cattle Part I: factors contributing to the development of digital dermatitis. Vlaams Diergeneeskd. Tijdschr. 2019, 88, 247-257.
97. *Wang H., Woolf C. J.*: Pain TRPs. Neuron 2005, 46, 9-12.
98. *Warnick L. D., Janssen D., Guard C. L., Gröhn Y. T.*: The effect of lameness on milk production in dairy cows. J. Dairy Sci. 2001, 84, 1988-1997.
99. *Watts K. M., Fodor C., Beninger C., Lahiri P., Arrazuria R., Buck J. De, Knight C. G., Orsel K., Barkema H. W., Cobo E. R.*: A differential innate immune response in active and chronic stages of bovine infectious digital dermatitis. Front. Microbiol. 2018, 9.
100. *Watts K. M., Lahiri P., Arrazuria R., De Buck J., Knight C. G., Orsel K., Barkema H. W., Cobo E. R.*: Oxytetracycline reduces inflammation and treponeme burden whereas vitamin D_3 promotes β-defensin expression in bovine infectious digital dermatitis. Cell Tissue Res. 2020, 379, 337-348.
101. *Weber J., Richter S., Freick M.*: Comparison of the therapeutic efficacy of salicylic acid paste with a polyurethane wound dressing for the treatment of digital dermatitis lesions in dairy cows. Res. Vet. Sci. 2019, 125, 7-13.
102. *Wells S. J., Garber L. P., Wagner B. A.*: Papillomatous digital dermatitis and associated risk factors in US dairy herds. Prev. Vet. Med. 1999, 38, 11-24.
103. *Werven T. van, Wilmink J., Sietsma S., van den Broek J., Nielen M.*: A randomized clinical trial of topical treatments for mild and severe udder cleft dermatitis in Dutch dairy cows. J. Dairy Sci. 2018, 101, 8259-8268.
104. *Wilson-Welder J. H., Alt D. P., Nally J. E.*: The etiology of digital dermatitis in ruminants: recent perspectives. Veterinary Medicine : Research and Reports 2015, 6, 155.
105. *Yamamoto T., Manabe H., Misawa N., Yamazaki W., Takahashi M., Okada K.*: Combination effect of allyl isothiocyanate and hoof trimming on bovine digital dermatitis. J. Vet. Med. Sci. 2018, 80, 1080.
106. *Yang D. A., Johnson W. O., Müller K. R., Gates M. C., Laven R. A.*: Estimating the herd and cow level prevalence of bovine digital dermatitis on New Zealand dairy farms: A Bayesian superpopulation approach. Prev. Vet. Med. 2019, 165, 76-84.

Corresponding author: Paulina Kaźmierczak, DVM; e-mail: paulina.kaz00@gmail.com