Biochemical and histopathological changes related to the topical application of Aloe vera ointment for canine pyoderma

Ali Arbaga1, Amanallah El-Bahrawy2, Ahmed Elsify1, Hadeer Khaled1, Hany Youssef Hassan1 and Ahmed Kamr1

1. Department of Animal Medicine and Infectious Diseases, Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt; 2. Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt.

Corresponding author: Hany Youssef Hassan, e-mail: hany.youssef@vet.usc.edu.eg
Co-authors: AA: ali.a.aazem@vet.usc.edu.eg, AE: amanallah.elbahrawy@vet.usc.edu.eg, AHe: ahmed.elsify@vet.usc.edu.eg, HK: hadeer.khaled@vet.usc.edu.eg, AK: ahmed.basha@vet.usc.edu.eg

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Abstract

Background and Aim: Pyoderma is common in dogs, and its treatment requires a novel medication rather than antibiotic therapy. This study aimed to determine the biochemical and histopathological changes associated with the topical application of Aloe vera 20% and 40% ointments, compared with gentamicin 0.1% ointment, in dogs suffering from Staphylococcus aureus pyoderma.

Materials and Methods: Serum and skin samples were collected from a negative control group before inducing pyoderma and from other subdivided groups on the 3rd, 7th, 10th, and 14th days post-inoculation for biochemical and histopathology examination.

Results: Serum aspartate aminotransferase, alanine aminotransferase (ALT), urea, and creatinine concentrations were higher in the positive control dogs on the 3rd day without treatment (DWT) compared with the negative control dogs (p<0.05). Compared with the healthy control dogs, serum zinc concentrations were lower in the positive control group on the 3rd, 7th, and 10th. Serum AST and ALT and skin zinc concentrations were lower in the positive control dogs on the 3rd, 7th, and 10th DWT and in dogs treated with A. vera 20% and gentamicin 0.1% ointments on the 3rd and 7th days post-treatment (p<0.05). Grossly, skin had erythema, pruritus, and pus-filled pustules of the untreated group. Microscopically, skin showed epidermal necrosis and edema, dermal collagen necrosis, and severe neutrophilic infiltration.

Conclusion: Compared with A. vera 20% and gentamicin 0.1% ointments, the topical application of A. vera 40% ointment-induced quicker skin healing and decreased the inflammatory changes caused by S. aureus inoculation, based on biochemical and histopathological changes reflective of its curative efficiency. A. vera 40% ointment may be a suitable alternative to antibiotics for the treatment of staphylococcal pyoderma in dogs.

Keywords: Aloe vera biochemical and histopathology examination, gentamicin, pyoderma, Staphylococcus aureus.

Introduction

Aloe vera belongs to the Asphodelaceae (Liliaceae) family. It is naturally cultivated throughout Africa, Asia, Europe, and America in tropical or subtropical regions. A. vera is registered as a medicinal drug of herbal origin in Egypt, India, Greece, Rome, and China [1]. A. vera extract consists of two primary parts: Latex and gel. A. vera gel is composed of 98.5-99.5% water, and the remaining dry matter contains more than 75 biologically active ingredients [2,3], which are helpful for the treatment of diseases. Major A. vera components include anthraquinones, polysaccharides, vitamins, enzymes, and low-pollutant components [4]; because of these components, A. vera has anti-inflammatory, immunomodulatory, wound healing, antiviral, antifungal, antitumor, antidiabetic, and antioxidant properties [5].

Canine pyoderma is a common disease, and staphylococcal folliculitis is the most frequently observed type in dogs [6-8]. Canine pyoderma is mainly caused by S. intermedius [6]; however, up to 10% of cases can be caused by Staphylococcus aureus and a recent emergent strain Staphylococcus schleiferi [6,8]. Antibiotic therapy, either locally applied or injected, is the usual protocol for treating staphylococcal pyoderma [6,7,9,10]. S. aureus can acquire resistant genes and overcome the inhibitory effects of antibiotics through several resistance mechanisms [11]. However, the potential role of A. vera in the treatment of canine staphylococcal pyoderma requires further investigation.

Several antibiotics are traditionally used to treat S. aureus, one of which is aminoglycoside gentamicin [11]. Gentamicin used to treat S. aureus infections by binding with the 30S ribosomal subunit and
inhibiting bacterial protein synthesis; its efficiency has decreased as the bacteria have acquired resistance encoded by mobile genetic elements [12]; therefore, treatment with gentamicin has begun to have a low value. Thus, there is a need to find an additional product for the treatment of staphylococcal pyoderma, particularly if this product is cheap, readily available, and of a natural source.

This study aimed to evaluate the biochemical and histopathological changes related to the topical application of A. vera ointment as a potential new treatment and compared its effects to those of a traditional treatment (gentamicin ointment) in dogs suffering from pyoderma. We hypothesized that, as a medicinal plant, A. vera would have a beneficial effect compared with gentamicin in treating staphylococcal pyoderma in dogs based on biochemical and histopathological assessments.

Materials and Methods

Ethical approval

All procedures in this study were approved by the University of Sadat City for the Care and Use of Animals in Education and Scientific Research (Approval code VUSC-007-1-19).

Study period and location

This study was carried out from September 2018 to May 2019. The experiment was carried out at the Department of Animal Medicine and Infectious Diseases, University of Sadat City.

Animals

Twenty 2-3-year-old male dogs were housed for 2 weeks to acclimatize to individual cages (120 cm×140 cm×160 cm (width×height×depth)) and had free access to food and water. Ivermectin 1% [Paramectin®, Pharma Swede, Egypt] was used for deworming by SC injection at a dosage of 10 mg/50 kg in compliance with manufacturer’s guidelines [13].

Experimental design

Each dog’s fur was shaved, and the skin was washed with sterile water and soap. Under local anesthesia, dogs were intradermally inoculated with 1 ml broth containing 10⁵ colony-forming unit of S. aureus RMSA4 strain as previously described [13,14]. Three days after inoculation, skin pyoderma appeared. To confirm the identity of the observed skin lesions, on the 3rd day post-inoculation, lesions were swapped for the identification of the grown colonies, on the 3rd day after the appearance of pyoderma) and on the 3rd, 7th, 10th, and 14th days post-treatment (DPT).

Tissue sampling and histopathology procedures

Punch biopsies (5 mm) were collected on day 0 (the 3rd day after the appearance of pyoderma) and on the 3rd, 7th, 10th, and 14th days post-treatment (DPT). Biopsy samples were preserved for 3 days in 10% neutral buffered formalin and then routinely processed and embedded in paraffin blocks. Paraffin tissue sections (4 µm) were cut, dried, and stained with hematoxylin and eosin stain for examination under a light microscope [18]. Sections were semiquantitatively scored as follows: −, none; +, mild < 25%; ++, moderate < 50%; and ++++, severe > 50% of examined sections. Six sections were examined and counted from the skin of each dog.
Statistical analysis
Data normality was assessed using a Shapiro–Wilk test; data were normally distributed and expressed as mean with standard error. A one-way analysis of variance was used to compare differences between the groups using IBM SPSS statistics version 16 (IBM Corporation, NY, USA) [19]. Significance was considered at p<0.05.

Results
Isolation and identification of *S. aureus* bacteria from dog lesions
The inoculated strain was confirmed through lesion swab cultures on Baird–Parker agar. Growing colonies were black, convex, and shiny and measured 1-1.5 mm in diameter with clear margins, which are characteristic of *S. aureus* (Figure-1). In addition, grapelike Gram-positive cocci appeared on Gram-stained smears under the microscope. The isolated strain showed the biochemical reactions, which are characteristic of *S. aureus*, as shown in Table-1.

Serum AST, ALT, BUN, creatinine, glucose, and zinc concentrations
Biochemical profiles revealed elevated serum AST and ALT concentrations in infected dogs on the 3rd day without treatment (DWT) compared with negative control dogs (p<0.05); however, there were no differences in the AST and ALT concentrations of dogs treated with *A. vera* 20% and 40% and gentamicin 0.1% at all time points compared with negative control dogs (p>0.05; Table-2). Serum BUN and creatinine concentrations were only lower in untreated infected dogs on the 3rd and 7th DWT. Serum glucose concentrations also decreased in dogs treated with *A. vera* 20% ointment on the 3rd DPT compared with negative control dogs (p<0.05), but these concentrations were no different from those of dogs treated with *A. vera* 40% and gentamicin 0.1% ointments (p>0.05; Table-2).

Gross examination
Compared with the positive control, treatment with *A. vera* 40% ointment induced faster healing than treatment with *A. vera* 20% and gentamicin 0.1% ointments; the healing effect of *A. vera* 20% ointment was equal to that of gentamicin 0.1%. The lesion scores for the untreated and treated groups are summarized in Table-3. Grossly, skin displayed signs of inflammation, such as erythema, pruritus, and pus-filled pustules. On day 0 of the experiment, the skin of all inoculated dogs was hyperemic, painful, and pruritic with excessive whitish thick pus-filled pustules (Figure-2a). On the 3rd DWT, dogs in the untreated group had severe forms of the aforementioned signs; whereas dogs treated with *A. vera* 20% and 40% and gentamicin 0.1% ointments had moderate pruritus and a moderate amount of pus (Figures-3a-c). On the 7th DWT, dogs in the untreated group continued to have these severe signs, whereas dogs treated with *A. vera* 20% and gentamicin 0.1% ointments also had moderate pruritus and a moderate amount of pus; on the other hand, dogs treated with *A. vera* 40% ointment had only a few amounts of pus on 7th DPT (Figures-3d-f). On the 10th DWT, untreated dogs had moderate pruritus and a moderate amount of pus (Figure-2b), whereas dogs treated with *A. vera* 20% and gentamicin 0.1% ointments had small amounts of pus, and dogs treated with *A. vera* ointment 40% showed epidermal collarette and an absence of pus (Figures-3g-i). On the 14th DWT, untreated dogs had moderate pruritus, a moderate amount of pus, and

Table-1: Biochemical reactions of isolated *S. aureus* from dogs’ pyoderma.

| Biochemical test | Isolated strain |
|------------------|-----------------|
| Oxidase          | –               |
| Catalase         | +               |
| Coagulase        | +               |
| DNase            | +               |
| Hemolysis        | +               |
| Pigment production | +   |
| Alkaline phosphatase | +   |
| Urease           | +               |
| Mannitol         | +               |
| Maltoolose fermentation test | + |
| Novobiocin 5mcg  | Sensitive       |
| Polymix n B 300- unit disc | Resistant |

*S. aureus* = *Staphylococcus aureus*
### Table-2: Biochemical profile of experimentally induced pyoderma in dogs treated by Aloe vera 20%; 40%; and gentamicin 0.1% ointments.

| Variables | ALT (U/L) | AST (U/L) | Urea (mmol/l) | Creatinine (mg/dl) | Zinc (μmol/L) | Glucose (mmol/L) |
|-----------|-----------|-----------|---------------|-------------------|---------------|-----------------|
| Control negative (before induction) (n=20) | 34.6±1.82a | 36.8±0.8a | 7.28±0.6a | 0.82±0.3a | 18.2±1.2a | 4.8±0.4a |
| Infected dogs without treatment (n=5) | | | | | | |
| 3rd DWT | 46.28±0.9b | 48.7±2.2b | 12.2±0.8b | 1.4±0.6b | 11.8±0.6b | 2.8±0.4b |
| 7th DWT | 35.5±0.8a | 38.2±1.2a | 11.6±0.4a | 1.2±0.7a | 12.7±0.8a | 3.2±1a |
| 10th DWT | 34.8±1.08a | 36.4±2.08a | 8.6±0.6b | 0.88±0.5a | 12.6±1.1a | 4.2±0.8a |
| 14th DWT | 36.04±0.5a | 36.68±1.3a | 8.24±0.6a | 0.82±0.4a | 16.8±0.6a | 4.6±0.6a |
| Dogs treated with Aloe vera gel ointment 20% (n=5) | | | | | | |
| 3rd DPT | 37.4±0.68a | 36.2±1.4a | 8.2±0.58a | 0.84±0.8a | 12.2±1.2a | 4.2±0.4a |
| 7th DPT | 34.8±1.1a | 38.4±0.8a | 8.08±0.8a | 0.82±0.3a | 12±0.5a | 4.0±3a |
| 10th DPT | 36.2±0.8a | 38.6±1.1a | 7.2±1.06a | 0.88±0.4a | 16.0±0.8a | 4.5±0.3a |
| 14th DPT | 34.12±0.8a | 37.2±0.6a | 8.0±0.4a | 0.78±0.6a | 18±1.06a | 4.18±0.4a |
| Dogs treated with A. vera gel ointment 40% (n=5) | | | | | | |
| 3rd DPT | 36.08±0.4a | 36.8±1.18a | 8.4±0.4a | 0.85±0.2a | 13.2±0.8a | 4.3±0.7a |
| 7th DPT | 36.4±0.38a | 37.08±0.6a | 8.7±1.02a | 0.82±0.4d | 17.4±1.2a | 4.8±0.3a |
| 10th DPT | 34.2±0.8a | 35.8±0.8a | 8.02±0.54a | 0.88±0.6a | 18.2±0.6a | 4.2±0.6a |
| 14th DPT | 34.7±0.6a | 36.6±1.04a | 7.6±0.4a | 0.80±0.3a | 18.4±0.6a | 4.6±0.4a |
| Dogs treated by gentamicin sulfate ointment 0.1% (n=5) | | | | | | |
| 3rd DPT | 36.12±0.4a | 35.8±0.4a | 7.85±0.4b | 0.88±0.4c | 12.28±0.6b | 4.2.8±0.6c |
| 7th DPT | 34.4±0.68a | 36.8±0.6a | 8.06±0.5a | 0.84±0.2a | 13.2±0.8a | 4.8±0.8a |
| 10th DPT | 35.42±0.5a | 37.24±0.8a | 8±0.68c | 0.78±0.5a | 17.2±0.5a | 4.6±0.2a |
| 14th DPT | 34.8±0.62a | 36.2±1.2a | 8.24±0.4a | 0.82±0.4a | 18±1.06a | 4.2±0.7a |

n=Number. Means with different letter superscripts in the same column are significantly different at (p<0.05).

A. vera=Aloe vera, ALT=Alanine aminotransferase, AST=Aspartate aminotransferase, DWT=Day without treatment, DPT=Days post-treatment.

### Table-3: Gross lesions score of experimental infection of dog skin with S. aureus and topical treatment with A. vera 20%, 40%, and gentamicin 0.1% ointments.

| Time | Gross lesions score |
|------|---------------------|
| Untreated group | A. vera 20% ointment | A. vera 40% ointment | Gentamicin 0.1% ointment |
| Zero day | 0 | 0 | 0 |
| 3rd DPT | 1 | 1 | 1 |
| 7th DPT | 0 | 1 | 2 |
| 10th DPT | 1 | 2 | 3 |
| 14th DPT | 1 | 3 | 4 |

DPT=Days post pyoderma treatment,
Lesions score: 0=Erythema, severe pruritis and pus-filled pustules filled with much pus, 1=Moderate pruritis and pustules filled with moderate amount of pus, 2=Mild pruritis and pustules with little pus, 3=Absence of pus and epidermal collarette, 4=Complete healing. A. vera=Aloe vera, S. aureus=Staphylococcus aureus, DPT=Days post-treatment.

the beginning of scar formation (Figure-2c), whereas dogs treated with A. vera 20% and gentamicin 0.1% ointments had epidermal collarette and an absence of pus, and dogs treated with A. vera ointment 40% showed complete healing and a complete absence of inflammatory signs (Figures-3j-l).

**Histopathological examination**

Microscopically, the topical application of A. vera 40% ointment induced faster skin healing and decreased the inflammatory changes caused by S. aureus inoculation than A. vera 20% and gentamicin 0.1% ointment. The results are summarized in Table-4. On day 0 of the experiment (the 3rd day after the appearance of lesions), skin showed epidermal necrosis and edema, dermal collagen necrosis, and severe inflammatory cells infiltration, mainly with neutrophils in the epidermis, dermis, and around the...
hair follicles (Figure-4a). Inflammation was deeply extended to involve subcutaneous fat and blood vessels. These neutrophilic infiltrations were present as either aggregate or in a diffuse manner in both the epidermis and dermis. On the 3rd DWT, the epidermis and dermis of untreated dogs had severe necrosis, edema, and neutrophilic infiltration diffusely observed around hair follicles and blood vessels (Figure-4b). On the 3rd DWT, dogs topically treated with A. vera 20% ointment and gentamicin 0.1% had moderate inflammatory changes in the epidermis and severe inflammatory changes in the dermis and subcutaneous tissue, whereas dogs topically treated with A. vera 40% ointment had moderate inflammatory changes throughout

Figure-3: Treated group. On 3rd days post-treatment (DPT), (a) Skin treated with Aloe vera ointment 20% showed erythema, pus filled pustules. (b) Skin treated with A. vera ointment 40% showed erythema, pruritis, and presence of pus. (c) Skin treated with gentamicin 0.1% showed erythema and whitish pus content. On 7th DPT, (d) skin treated with A. vera ointment 20% showed erythema with moderate pus content. (e) Skin treated with A. vera ointment 40% showed erythema with less pus content. (f) Skin treated with gentamicin ointment 0.1% showed erythema and moderate pus content. On 10th DPT, (g) skin treated with A. vera ointment 20% showed small amounts of pus. (h) Skin treated with A. vera ointment 40% showed epidermal collarette with absence of pus. (i) Skin treated with gentamicin ointment 0.1% showed little pus. On 14th DPT, (j) skin treated with A. vera ointment 20% showed epidermal collarette with absence of pus. (k) Skin treated with A. vera ointment 40% showed complete healing. (l) Skin treated with gentamicin ointment 0.1% showed epidermal collarette. Lesions are indicated by arrows.
all skin layers (Figure-5c). On the 7th DWT, inflammatory changes, folliculitis, and subcutaneous blood vessel inflammation were severe in the skin of dogs from the untreated group (Figure-4c). On the 7th DWT, dogs topically treated with A. vera 20% ointment and gentamicin 0.1% showed moderate necrosis, infiltration of neutrophils, and few lymphocytes in the epidermis and dermis, whereas these changes were severe in the subcutaneous tissue, including blood vessels. On the 7th DWT, dogs topically treated with A. vera 40% ointment showed mild neutrophilic infiltration that was focal in the epidermis and dermis and moderate neutrophilic infiltration that was diffuse in the subcutaneous tissue (Figures-5d-f). On 10th DWT, inflammatory changes, including necrosis, neutrophilic infiltration, folliculitis, and subcutaneous fat and blood vessel inflammation, were severe and diffuse throughout all skin of dogs in the untreated group (Figure-4d). On the 10th DPT, the epidermis and dermis of dogs topically treated with A. vera 20% and gentamicin 0.1% ointments demonstrated mild neutrophilic infiltration, whereas the subcutaneous tissue showed moderate inflammation and necrosis. On the 10th DPT, dogs topically treated with A. vera 40% ointment showed an absence of inflammation in the epidermis, whereas inflammation was mild in the dermis and subcutaneous tissue (Figures-5g-i). On the 14th DWT, in the untreated group, inflammatory changes, including necrosis and neutrophilic infiltration were moderate in the epidermis, dermis, and subcutaneous tissue (Figure-4e). On the 14th DPT, the epidermis and dermis of dogs topically treated with A. vera 20% ointment demonstrated

Table-4: Histopathology scoring of dog’s skin inflammation and its location after experimental inoculation with S. aureus and topical treatment with A. vera 20% and 40% and gentamicin 0.1% ointments.

| Group         | Untreated        | A. vera 20% ointment | A. vera 40% ointment | Gentamicin 0.1% ointment |
|---------------|------------------|----------------------|----------------------|-------------------------|
|               | Epid  | Der | S/C | Epid | Der | S/C | Epid | Der | S/C | Epid | Der | S/C |
| Zero day      | +++   | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++ |
| 3rd DPT       | +++   | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++ |
| 7th DPT       | +++   | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++ |
| 10th DPT      | +++   | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++  | +++ | +++ | +++ |
| 14th DPT      | +++   | +++ | ++  | –     | –   | –   | –    | –   | –   | –    | –   | +   | + |

DPT=Days post pyoderma treatment, Epid=Epidermis, Der=Dermis, S/C=Subcutaneous tissues including fat and blood vessels. Scoring of histopathology (edema, necrosis, mononuclear cell infiltration and folliculitis); –: None; +: Mild <25%; ++: Moderate <50%; +++: Severe >50% of examined sections. A. vera=Aloe vera, S. aureus=Staphylococcus aureus

Figure-4: Untreated group. (a) On zero day of the experiment, the skin showing epidermal necrosis dermal collagen necrosis and severe neutrophil infiltration in the epidermis, dermis, and around the hair follicles; H and E 20×. (b) On 3rd day without treatment (DWT), the skin showed severe necrosis and neutrophil infiltration; H and E 40×. (c) On 7th DWT, the skin has severe inflammation in the subcutaneous fat and arteritis; H and E 10×. (d) On 10th DWT, the skin showing inflammatory cells invades the hair follicles; H and E 20×. (e) On 14th DWT, the skin showing moderate inflammatory cells in the subcutaneous tissue; H and E 20×.
no inflammation, whereas the subcutaneous tissue showed mild inflammation, and the epidermis of dogs topically treated with gentamicin 0.1% had no inflammation, whereas the dermis and subcutaneous tissue showed mild inflammation. Finally, on the 14th DPT, dogs topically treated with A. vera 40% ointment had complete skin healing and an absence of inflammatory signs in all skin layers (Figures-5j-l).

Figure-5: Treated group. On 3rd days post-treatment (DPT), (a) skin treated with Aloe vera ointment 20% showed epidermal necrosis, edema, severe neutrophilic infiltration, and hair folliculitis; H and E 10×. (b) Skin treated with A. vera ointment 40% showed epidermal necrosis, edema, and moderate neutrophilic infiltration; H and E 10×. (c) Skin treated with gentamicin ointment 0.1% showed epidermal necrosis, edema, severe neutrophilic infiltration, and hair folliculitis; H and E 10×. On 7th DPT, (d) Skin treated with A. vera ointment 20% showed focal suppurative inflammation in the subcutaneous fat; H and E 10×. (e) Skin treated with A. vera ointment 40% showed epidermal necrosis with few neutrophilic infiltration; H and E 4×. (f) Skin treated with gentamicin ointment 0.1% showed diffuse suppurative inflammation in the epidermis and subcutaneous fat; H and E 4×. On 10th DPT, (g) skin treated with A. vera ointment 20% showed mild inflammation in the dermis and around the hair follicles; H and E 10×. (h) Skin treated with A. vera ointment 40% showed mild inflammatory zone in the dermis; H and E 10×. (i) Skin treated with gentamicin ointment 0.1% showed mild inflammation around the hair follicles; H and E 10×. On 14th DPT, (j) skin treated with A. vera ointment 20% showed normal histological architecture of skin; H and E 4×. (k) Skin treated with A. vera ointment 40% showed normal histological architecture of skin; H and E 4×. Lesions are indicated by arrows.
Discussion

In the present study, the indicators of liver function (i.e., AST and ALT levels) and kidney function (e.g., BUN and creatinine) were higher in dogs experimentally infected with pyoderma; our results are similar to those reported for dogs with pyoderma and dermatophytosis [20] but disagree with the results of other studies [21,22]. The increased concentrations of BUN and creatinine may be due to dehydration caused by the hemorrhagic conditions revealed from pyoderma lesions, whereas the increased levels of AST and ALT may be related to increased levels of inflammatory cytokines, as reported in a previous study by our group [13]. Serum glucose concentrations were lower in the experimentally infected dogs compared with those of negative control dogs; these findings are in line with those previously documented in dogs [21]. Biochemical profiles revealed in the positive control group, making our results generally consistent with those of a previous study of dogs with atopic dermatitis [23]. Zinc plays a significant role in preserving lipid membranes against oxidation; thus, low zinc concentrations may act as a potential mechanism against reactive oxygen species production [24].

In this study, pyoderma appeared 3 days after inoculation; this differs from other studies, which describe the appearance of lesions 24 h after inoculation [25]. This variation may be due to differences with respect to the inoculated strain or the dogs’ age and breed. In terms of depth, canine pyoderma is divided into superficial bacterial folliculitis and deep pyoderma, including subcutaneous tissue, fat, and blood vessels [7,9,10]. Interestingly, both types of pyoderma were observed, with inflammation in hair follicles and deep in the subcutaneous tissue, causing cellulitis and panniculitis. Deep pyoderma has been reported to be more serious than superficial pyoderma [9].

Systemic antimicrobial treatment of pyoderma induces multidrug resistance. In addition, in some countries, the use of some antibiotics is limited in pets [9,10]. As such, topical treatment may be the most appropriate method for treating pyoderma in dogs [10]. A. vera is a natural plant rich in anthraquinones, polysaccharides, and pyrocatechol, a hydroxylated phenol. Anthraquinones have a similar action as tetracycline: The inhibition of bacterial protein synthesis [26]. Polysaccharides stimulate leukocyte phagocytic activity to kill bacteria [27]. Pyrocatechol has a toxic effect on microorganisms [28]. Through these components and others, as seen in this study, the topical application of A. vera ointment successfully induces skin healing and resolves the inflammatory changes caused by S. aureus inoculation, as confirmed by histopathology. In addition, A. vera ointment was able to treat deep pyoderma, which involved fat and blood vessels in the subcutaneous tissue. A. vera 40% ointment treated skin pyoderma more quickly than A. vera 20% and gentamicin 0.1% ointments; this may be explained by a dose-dependent concentration, as previous research has shown that high concentrations of several dilutions of A. vera extract can successfully inhibit S. aureus [29]. Moreover, in vitro assays previously confirmed the inhibitory effect of A. vera ointment on bacteria [30,31].

Conclusion

Based on the biochemical and histopathological improvement of skin lesions, the topical application of A. vera 40% ointment may be a suitable herbal therapy against staphylococcal pyoderma in dogs. As such, A. vera 40% ointment is a suitable therapy, without the side effects associated with antibiotics, for use in the veterinary field.

Authors’ Contributions

HYH: Designed the idea and experiment. AK, AA, AE, AhE, and HK: Executed the experiments and analyzed the samples. AK, AA, and AE: Interpreted the data and drafted the manuscript. AE: Histopathological part. AhE: Responsible for bacteriological share. AA and HK: Biochemical part. AK: Responsible for gel formation, statistical analysis and editing of the manuscript. All authors critically revised the manuscript for important intellectual content. HYH: Supervised the study. All authors read and approved the final manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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