

## Open-label Clinical Study

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### **Safety and Efficacy of Topical Antimicrobial Products: Forticept® Blue Butter™ Antimicrobial Gel and Forticept® Maxi Wash™ Antimicrobial Cleanser in Therapeutic Management of Canine Superficial Pyoderma: an open-label pilot study.**

10 Patient Study

#### **Abstract**

Ten dogs affected with superficial pyoderma were treated twice daily with Forticept® Maxi Wash™ spray and Forticept® Blue Butter™ antimicrobial gel, as well as with Forticept® Forteclenz™ shampoo twice weekly. Clinical diagnosis of canine superficial pyoderma was based on history, clinical signs and skin cytology. Some of the patients were previously treated with multiple systemic therapeutic modalities including topical antimicrobials/antibiotics with little or no effect. There were no local side effects observed during the topical therapy with majority of dogs having complete resolution after 20-30 days.

Keywords: Canine; pyoderma; Forticept® Blue Butter™; Forticept® Maxi Wash™, Forticept® Forteclenz™

#### **INTRODUCTION**

Canine superficial pyoderma, defined as a superficial bacterial infection of the epidermis and hair follicle, is more common in the dog than any other mammalian species.<sup>1</sup> Several reports support the clinical impression that canine pyoderma appears to be a common diagnosis with a prevalence of up to 5% in private practices within USA.<sup>2,3</sup> Clinical consequences for individual affected dogs and the scale of disease-burden at a population level are both of concern when considering the overall impact of pyoderma on canine welfare. The condition is frequently recurrent and causes varying degrees of pain and pruritus depending on the extent of lesions.<sup>1</sup> Coagulase-positive bacteria *Staphylococcus (S.) pseudintermedius* is the major pathogen associated with canine superficial pyoderma and *S. schleiferi* strains has been recently recognized as another causative agent.<sup>1</sup> Recently, multidrug resistant canine superficial pyoderma strains of *S. pseudintermedius* and *S. schleiferi*, refractory to treatment by most commonly used classes of antibiotics including methicillin, have emerged and disseminated widely in USA and Europe<sup>4</sup> and represent a major challenge for small animal practitioners and veterinary dermatologists. The widespread emergence of multidrug-resistant staphylococci has advocated even greater interest for the use of targeted topical antimicrobial therapy, as sole or adjuvant therapy in dogs with pyoderma.

## History

Total of 10 dogs of varying breeds and sexes (4 female and 6 male) were diagnosed with superficial pyoderma; skin lesions consisted of erythematous macules with crusts, pustules, epidermal collarettes. In three dogs, clinical signs of ulcerations and draining tracts were suggestive of folliculitis/furunculosis deep pyoderma lesions.

## Materials and Methods

Dogs were diagnosed with superficial bacterial pyoderma based on the history, clinical signs and lesional skin cytology revealing cocci.<sup>5,6</sup> All dogs were treated with topical Forticept® shampoo twice weekly (10-15 minute exposure time) and Forticept® Blue Butter™ Antimicrobial Gel and Forticept® Maxi Wash™ once or twice daily until condition is resolved.

Dogs with superficial pyoderma should be treated only with topical antimicrobial therapy such as the shampoo baths 2 to 3 times per week until clinical resolution. Dogs with clinical signs of deep pyoderma commonly require systemic antibiotics and daily topical antimicrobial therapy. Shampooing removes bacteria, crusts, and scales, and reduces itching, odor, and oiliness. Clinical improvement and resolution of superficial pyoderma with topical antimicrobial therapy may take up to 4-5 weeks.

Forticept® Blue Butter™ Antimicrobial Gel (Hydrogel) – is a novel FDA registered OTC (Over-the-Counter) veterinary drug product. This product is based on proprietary polyacrylate polymer technology that improves the efficacy and bioavailability of its active ingredients Benzethonium Chloride and Thymol in concentrations that have clinical evidence of safety and efficacy as topical antimicrobial agents. Product claims are in line with claims allowed under the monograph for these ingredients.

Forticept® Maxi Wash™ Antimicrobial Skin and Wound Treatment (Liquid Spray) - is a novel FDA registered OTC (Over-the-Counter) veterinary drug product. This product is also based on proprietary polyacrylate polymer technology that improves the efficacy and bioavailability of its active ingredient Benzalkonium Chloride in concentration that has existing clinical evidence of safety and efficacy as topical antimicrobial agent. Product claims are in line with claims allowed under the monograph for this excipient.

Forticept® Forteclenz™ shampoo – product developed by Lidan, Inc., specifically for this study. It is a medicated shampoo based on Bezalkonium Chloride 0.13% and the same polymer technology as Forticept® Blue Butter™ Gel and Forticept® Maxi Wash™.

All products in this study claim to be non-toxic and have broad spectrum antimicrobial activity; and the efficacy was assessed and confirmed in separate *in vitro* and *in vivo* studies.

## Clinical Results

The topical treatment with Forticept® shampoo, Forticept® Blue Butter™ Antimicrobial Gel and Forticept® Maxi Wash™ revealed excellent tolerability as well as clinical resolution or reduction in superficial pyoderma clinical signs in all dogs. There were no signs of skin irritation, erythema, scaling or pruritus developing after the application of topical products in any dogs.

## Patient's Details

### *Dog 1 Zoey*

Dog 1, a 9 year old female spayed Collie, presented with generalized superficial pyoderma not responding to chlorhexidine shampoo and twice weekly baths. She has history of having borreliosis and incontinence. Her skin lesions consist of widespread generalized epidermal collarrettes with erythematous margins and sever crusting. The skin cultures from epidermal collaret lesions revealed antibiotic resistant *Staphylococcus pseudintermedius* and *Staphylococcus schleiferi*. She was treated topically with Forticept® Maxi Wash™ spray followed with Forticept® Blue Butter™ gel twice daily, as well as Forticept® shampoo twice weekly and her skin lesions resolved in 25 days of treatment. This patient was monitored after the resolution of initial condition. On the day 55 from the beginning of the treatment no recurrence was observed along with healthy hair growth. (Laboratory report is attached)

### *Dog 2 Rena*

Dog 2, a 9-year-old female spayed Collie, presented with generalized superficial pyoderma not responding to chlorhexidine shampoo and twice weekly baths. She has history of having borreliosis and incontinence. Her skin lesions consist of widespread generalized epidermal collarrettes with erythematous margins and sever crusting. The skin cultures from epidermal collaret lesions revealed antibiotic resistant *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, and *Proteus mirabilis*. She was topically treated with Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel twice daily and her skin lesions resolved in 21 days of treatment. (Laboratory report is attached)

### *Dog 3 Lucy*

Dog 3, a 11 year old female spayed Golden Retriever, presented with generalized superficial pyoderma not responding to chloramphenicol for 3 weeks. The skin cultures from skin pyoderma lesions revealed infection of multidrug resistant *Staphylococcus pseudintermedius* only sensitive to rifampin and Chloramphenicol antibiotics. However, the dog did not respond to 21 days course of Chloramphenicol antibiotics. The dog was given baths twice weekly with diluted bleach but that did not respond to this treatment.

At the next office visit the dog was started on the topical treatment with Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel twice daily, and Forticept® shampoo twice weekly. Her skin lesions resolved in 20 days. At the follow-on visit no recurrence was observed along with healthy hair growth. (Laboratory report is attached)

### *Dog 4 Moe*

Dog 4, a 8-year-old male neutered York terrier, was presented to the UGA Dermatology service on chronic superficial pyoderma of 1 year duration. Owner states that skin lesion began at one spot on the back about 2 years ago and then spread out throughout the back. According to the owner, Moe is constantly itchy throughout the day and tries to scratch his back. The skin cultures from epidermal collaret lesions revealed drug resistant *Staphylococcus pseudintermedius* and multidrug resistant *Staphylococcus schleiferi*.

He was treated with topical administration of Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel twice daily; his skin lesions improved within 10 days but the client pursued systemic antibiotic therapy after that. (Laboratory report is attached)

#### *Dog 5 UGF*

Dog 5 is a 3-year-old male castrated Beagle, that presented with acute moist erosive pododermatitis on hind right leg. He was severely itchy and painful on the lesions. The skin cytology revealed numerous rod and cocci-shaped bacteria.

He was treated with topical administration of Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel for 24 hours and the next day his skin lesions almost completely resolved; after an additional day of topical treatment all skin lesions are in complete remission.

#### *Dog 6 Maggie*

Dog 6 is a 15-year-old Female Spayed Maltese, presented with chronic superficial pyoderma affecting ventral thorax and abdomen. The dog has been severely itchy and non-responsive to Lokivetmab, an anti-IL31 monoclonal antibody used to treat pruritus in canine atopic patients. The skin lesions consisted of erythematous multifocal to coalescing papules and crusts and skin cytology revealed cocci-type bacteria; all signs suggestive of superficial staphylococcal pyoderma.

The patient was treated with topical administration of Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel once daily and Forticept® shampoo twice weekly (no systemic antibiotics were given); all skin lesions resolved within 18 days.

#### *Dog 7 Tommy*

Dog 7 is a 10-year-old male castrated Mixed Breed Dog, presented for chronic atopic dermatitis, secondary multidrug resistant staphylococcal superficial skin infection and deep staphylococcal infection with furunculosis and panniculitis. The patient had generalized lesions involving thorax and all four feet.

Due to multidrug resistant *Staphylococcus pseudintermedius* deep pyoderma, the dog was treated with systemic antibiotic Chloramphenicol, Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel once daily and Forticept® shampoo twice weekly. All skin lesions resolved after 40 days.

#### *Dog 8 Blu*

Dog 8 is a 13-year-old male neutered, American Pit Bull Terrier, presented with acute superficial staphylococcal skin infection and history of chronic atopic dermatitis that is currently controlled. The clinical skin lesions consisted of numerous small erythematous epidermal collarettes scattered over his entire trunk (all aspects including dorsum and axillary and groin areas).

The patient was treated with topical Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel once daily and Forticept® shampoo twice weekly (no systemic antibiotics were given); all skin lesions resolved within 25 days.

#### *Dog 9 Banks*

Dog 9 is a 6 year old male castrated Labrador Retriever presented with moderate chronic atopic dermatitis and staphylococcal superficial pyoderma on ventral and lateral thorax. The patient was treated with systemic antibiotic Clindamycin twice daily and topical Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel once daily. After 3 weeks, there were no signs of active infection on dorsum with occasional interdigital lesion still present.

#### *Dog 10 Oliver*

Dog 10 is a 6 year old male castrated English Bulldog presented with severe chronic atopic dermatitis and multidrug resistant staphylococcal superficial pyoderma on dorsal trunk. Furthermore, the patient experienced severe interdigital deep pyoderma.

Due to severity and deep pyoderma skin lesions, the patient was treated Forticept® Maxi Wash™ and Forticept® Blue Butter™ gel once daily and Fortecenz shampoo twice weekly (no systemic antibiotics were given). All skin lesions of superficial pyoderma resolved within 24 days.

### **Discussion**

Since the emergence of multi-drug resistant bacteria, including Staphylococcus, in humans and companion animals, antiseptics have gained much importance as an alternative to treatment with antibiotics. In this open-label study, topical products with benzethonium chloride, thymol, and benzalkonium chloride have shown excellent safety and antimicrobial activity against staphylococcal superficial pyoderma in dogs regardless of antibiotic resistance in bacteria.

There is no prior scientific evidence for *in vitro* and *in vivo* benzethonium and benzalkonium chloride antimicrobial efficacy in presented concentration in dogs when addressing superficial pyoderma caused by antibiotic resistant bacteria.

### **Conclusion**

Canine pyoderma is a common diagnosis in small animal practice and often leads to prescription of systemic antibiotics. A major part of scientific knowledge on pyoderma was compiled during the 1970s and 1980s, when treatment of bacterial skin infection presented relatively limited challenges. Nevertheless, the ability to treat canine pyoderma effectively is now significantly restricted by the emergence of multidrug-resistant, methicillin-resistant staphylococci (MRS) and other drug resistant pathogens. The threat from increasing occurrences of antimicrobial resistance and ability of bacteria to be transmitted from animals to humans, MRS opens a new dimension of public health implications to the management of canine pyoderma and compel to reassess best management strategies. This statement focusses on the impact of MRS on how canine pyoderma is managed now and how traditional treatment recommendations need to be updated in the interest of good antimicrobial stewardship.

The objective of this study was to assess safety and efficacy of novel topical products: Forticept® Blue Butter™ Antimicrobial Gel and Forticept® Maxi Wash™ in management and treatment of canine pyoderma and other skin conditions caused by pathogenic bacteria. Both products are found to be safe and did not cause any adverse reactions or worsening of the treated condition. Both products were found to be effective in treatment of canine pyoderma and resolution of skin lesions.

I would like to add that both products were easy to use both in clinical environment as well as in home environment by pet owners. All animals tolerated product application well without any change in normal behavior. Forticept® Maxi Wash™ practically has no odor and provided good skin cleansing prior to the application of the second product. Forticept® Blue Butter™ Antimicrobial Gel is non-greasy light blue hydrogel with pleasant thyme aroma. It applies and spreads easily on the animal skin and not causing any apparent discomfort on the affected areas. Both clinical staff and pet owners found Forticept® Forteclenz shampoo to be a valuable addition to the regimen due to good ability of surfactant system to eliminate dirt, oils, and malodor without over-drying the skin, as many medicated shampoos tend to have this effect.

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