Enhanced-Delivery Tetracycline for Wound Care and Post-Surgical Conditions

By: Dr. Christopher Otiko, ViaDerma, Inc.

Summary

Vitastem™ is an over-the-counter (OTC) topical ointment with a patent pending dual carrier delivery system that greatly enhances product penetration – the ViaDerma Transdermal Carrier (VTC) system. VTC permits rapid penetration of active ingredients through the skin and into cells, making this not only one strongest antibiotics in the world, but also giving it intense healing properties unlike anything else available on the market today. VTC enables tetracycline to overcome the bacteria's efflux pumps, and rather *influx* the antibiotic – this means that Vitastem has both a chemical *and* physical kill mechanism, which we call Advanced Biological Coverage (ABC).

Introduction

Vitastem was developed by a team of scientists and physicians with a combined experience of 60 years in Biochemistry, Molecular Biology, and Wound Care. Our novel approach to overcome drug resistance of antibiotics is designed to sustain the effectiveness of Vitastem for many years. This gives Vitastem a longer useful lifetime and therefore more commercial value. In recent years, the dearth of new antibiotics has been largely due to the uncertain new-drug commercial lifetime which is diminished when bacteria develop immunity to that drug.

"Gram Positive" vs "Gram Negative" Bacteria

The terms Gram-positive and Gram-negative are used to quickly classify bacterial into two broad categories according to their different types of cell walls. It refers to their results in the Gram stain test – gram positive bacteria give a positive result in the Gram stain test, because they take up the crystal violet stain and then appear to be purple colored when seen through a microscope; gram negative bacteria appear purple or pink because they take up the counterstain in this test.

All Gram-positive bacteria are bound by a single-unit lipid membrane, and, in general, they contain a thick layer (20–80 nm) of peptidoglycan responsible for retaining the Gram stain. In contrast to Gram-positive bacteria, all archetypical Gram-negative bacteria are bounded by a cytoplasmic membrane and an outer cell membrane; they contain only a thin layer of peptidoglycan (2–3 nm) between these membranes. The presence of inner and outer cell membranes defines a new compartment in these cells: the periplasmic space or the periplasmic compartment.

Despite their thicker peptidoglycan layer, Gram-positive bacteria are more receptive to antibiotics than Gram-negative, due to the absence of the outer membrane.

Antibiotic Resistance

It is well known that bacteria evolve to develop resistance to the effects of antibiotics. There are many types of antibiotics. Chiefly, they have two types of mechanism of action: antibiotics either function as bacteriostatic or as bactericidal. As bacteriostatic they stop the bacterium from multiplying further by interfering with their DNA, but they do not kill the bacteria. As bactericidal, they kill the bacteria (eg, Penicillin is a bactericidal antibiotic).[1]

A plasmid is a small, circular, double-stranded DNA molecule that is distinct from a cell's chromosomal DNA. Plasmids naturally exist in bacterial cells, and they also occur in some eukaryotes. Often, the genes carried in plasmids provide bacteria with genetic advantages, such as antibiotic resistance.[2]

It is relatively easy for bacteria to change their response to a chemical threat, but it takes numerous generations for bacteria to grow a new kind of cell wall structure to respond to a physical threat. This means that antibiotic products that utilize a physical mechanism of action show great potential for treating bacteria that develop resistance to standard antibiotics.

Active efflux is a mechanism responsible for extrusion of toxic substances and antibiotics outside the cell. This mechanism is important in medicine as it can contribute to bacterial antibiotic resistance - pathogens use an energy dependent mechanism (active transport) to pump antibiotics outside of their cell walls before the antibiotic is able to have an effect (kill the pathogen), rendering the antibiotic ineffective. Some efflux systems are drug-specific, whereas others may accommodate multiple drugs, and thus contribute to bacterial multidrug resistance (MDR). Efflux may be the most important evolutionary mechanism used by bacteria to develop resistance to antibiotics. Some of these efflux pumps exhibit an extremely wide specificity covering practically all antibiotics. It is disturbing to the medical community that the antibacterial agents of the most advanced type, which are unaffected by common resistance mechanisms, are the compounds whose use appears to select for multidrug-resistant mutants that overproduce these efflux pumps of wide specificity.[3]

Tetracycline

Tetracycline resistance is normally due to the acquisition of new genes often associated with either a mobile plasmid or transposon. Specific tetracycline resistance genes have been identified in 32 Gram-negative and 22 Gram-positive genera.[4]

As an antibiotic, tetracycline uses a *chemical* mechanism of action. Tetracycline antibiotics are protein synthesis inhibitors, inhibiting the binding of aminoacyl-tRNA to the mRNA-ribosome complex. They do so mainly by binding to the 30S ribosomal subunit in the mRNA translation complex.[5] As an anti-inflammatory, tetracycline suppresses the up-regulation of matrix metalloproteinases and cathelicidins, which are hallmarks of chronic inflammation. This has led to extensive research on chemically-modified tetracyclines or CMTs (like incyclinide) for the treatment of rosacea, acne, and various types of neoplasms.

Vitastem and How it Works

Our tetracycline technology provides enhanced capabilities against antibiotic-resistant strains of pathogens.

Advanced Biological Coverage (ABC) technology

Single chemicals offer limited enhancements of skin permeability. Mixtures of chemicals can overcome this limitation owing to their synergistic interactions. Vitastem utilizes an enhanced transdermal drug delivery system to transport key ingredient molecules quickly and effectively through the skin and into cells. It is unique in that it utilizes both a physical and a chemical mechanism of kill to fight pathogens – we call this Advanced Biological Coverage (ABC). All known antibiotics (other than ours) primarily use only a chemical mechanism of kill. To overcome bacteria's tendency to evolve and become resistant to an antibiotic, Vitastem additionally incorporates a physical kill mechanism. This is the reason why Vitastem's tetracycline technology provides enhanced capabilities against antibiotic-resistant strains of pathogens.

ViaDerma Transdermal Carrier (VTC)

Vitastem's transdermal penetration system (VTC), is a proprietary patent-pending method of delivering key ingredients. Individually, each of the FDA approved inactive ingredients are single chemicals that offer limited enhancements to skin permeability. However, when these ingredients are mixed at specific concentrations, with specific temperature and time, the cocktail of chemicals act synergistically to form an enhanced transdermal carrier system with superior product penetration. Our patent pending transdermal formulation then carries the active ingredient, tetracycline, deep into the tissue and across cell walls. This means that tetracycline penetrates in much higher concentrations and with greater effectiveness than other products. Whereas conventional topical antibiotics require more time (usually prescribed for 5 to 7 days for best results), Vitastem usually produces desirable results in 24 hours (or less). VTC increases the mass transfer of tetracycline across cell membranes, penetrating any cell wall, and enabling it to get where most products can't.

Topical Vs Oral Antibiotics

Vitastem topical antibiotic has been shown to kill all harmful Gram positive and Gram negative bacteria that have been available for testing (see SDSU study). We believe this is the world's strongest broad-spectrum topical antibiotic.

Liquid solutions are typically thought of as only being able to provide a limited dose, because they are applied as a thin topical application. However, a private study conducted by one of the inventors showed that after just 60 seconds, 58% of the Vitastem had penetrated the skin as deep as 0.125cm, with only 42% of the initial dose left on the surface of the skin. After 24 hours, there was 92% product penetration as deep as 0.6cm.

Conditions and Case Studies

Burns

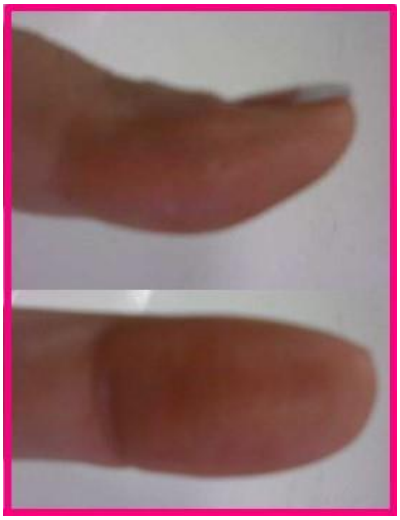
<u>Burn Case Study 1:</u>
Patient: A 38-year-old female, 2nd degree burn to thumb while cooking. Ice pack applied for a few minutes, obtained some pain relief.

Regimen: Physician friend was present and applied Vitastem.

Result: Patient reported that pain subsided from a “10” to a “3” within minutes following the topical application of Vitastem, and to a “zero” after two hours. After 12 hours, blister had resolved, no redness or inflammation, pain-free, no evidence of burn.

Before Vitastem application (just minutes after burn)

After 12 Hours of Treatment



After 24 Hours of Treatment

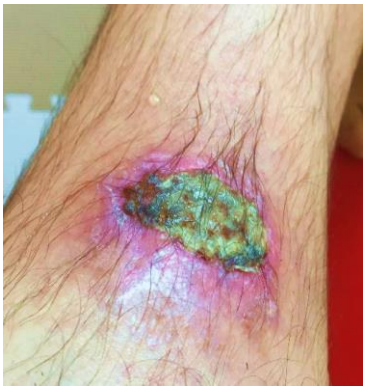
Burn Case Study 2:

Patient: Male, 42 years old, good health. Third degree burn to right calf, which became infected. Applied Triple Antibiotic for 2-weeks before consulting a physician and beginning Vitastem treatments.

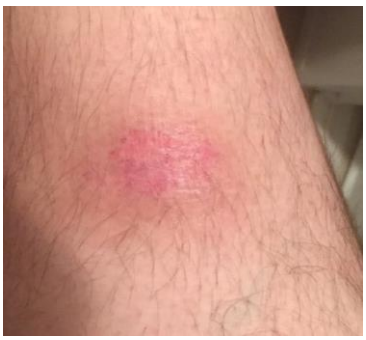
Regimen: 2-drops, 3-time per day, covered with non-sterile dry dressing

Result: Completely healed in 30 days with minimal scaring. Without Vitastem, patient would likely have been hospitalized due to infection.

Before Treatment



After 30 Days Treatment



Burn Case Study 3:
Patient: Male, 47 years old, Good health, **Second Degree Burn** from Ice Pack – applied to torn calf muscle and feel asleep.

Regimen: 2-drops, 3-time per day, cover with non-sterile dry dressing.

Result: Completely healed in 42 days with minimal scaring. (Muscle tear healed in 4-days). Typical healing cycle for this patient would have been 6-8 weeks but with significant scaring due to skin complexion.

Before and After Treatment

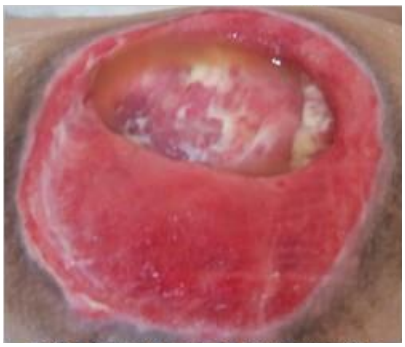
Wound Care

Wound Care Case Study 1:
Patient: diagnosed with Stage IV Decubitous Ulcer, Left Hip. Patient has been bedridden for years. A full-thickness tissue loss with extension into muscle, bone, tendon, and joint capsule of the left hip.

Result: In the follow up picture, 10 days later, the wound healing has progressed where the underlying fascia is now covered up by new subcutaneous growth.

Before

After 10 Days of Treatment



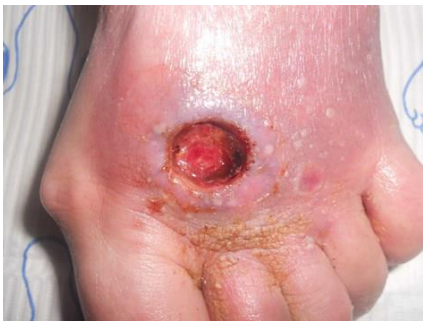
Wound Care Case Study 2:

Patient: Female, 93 years old, Diabetic, suspected cigarette Burn. Foot was cellulitic, Wound was 6 months old – doctors feared a fatal infection due to patient's age and co-morbidity (diabetes, peripheral vascular disease)

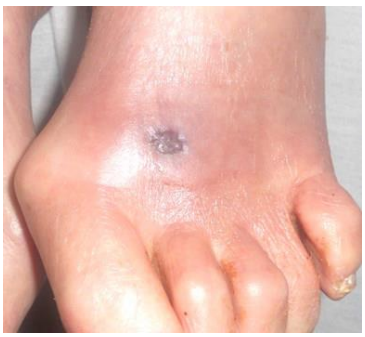
Regimen: 2-drops, 3-time per day, covered with non-sterile dry dressing

Result: Completely healed in 32 days with minimal scaring. Patient lived for another 6 years without any further problems with the foot. Without Vitastem, healing time would have been 3-4 months to patient age and health.

Before



Day 32



MRSA

Disclaimer: Vitastem is not marketed as a treatment for MRSA or staph infections in the USA.

The reason for this is that the FDA has NOT approved tetracycline or Vitastem for sale as a treatment for MRSA or staph infections. Nothing in this document (or any document or web site sponsored by ViaDerma Distribution) shall be interpreted as claiming or implying that our products are for sale in the USA for use as treatments for MRSA or staph infections.

The only way that any ViaDerma Distribution products, including Vitastem, can be used for treatment of MRSA or staph infections is if a physician elects to do that, based on NO marketing or sales of our products for that purpose in the USA.

All MRSA Case studies were off-label use, under physician supervision.

Methicillin-resistant Staphylococcus aureus (MRSA) is a gram-positive bacterium that is genetically different from other strains of Staphylococcus aureus. MRSA is responsible for several difficult-to-treat infections in humans. MRSA is any strain of S. aureus that has developed, through horizontal gene transfer and natural selection, multiple drug resistance to beta-lactam antibiotics. β-lactam antibiotics are a broad spectrum group which includes some penams – penicillin derivatives such as methicillin and oxacillin, and cephems such as the cephalosporins.[6] Strains unable to resist these antibiotics are classified as methicillin-susceptible Staphylococcus aureus, or MSSA.

MRSA is prevalent in hospitals, prisons, and nursing homes, where people with open wounds, invasive devices such as catheters, and weakened immune systems are at greater risk of nosocomial infection (hospital-acquired infection). MRSA began as a hospital-acquired infection, but has developed limited endemic status and is now community-acquired as well as livestock-acquired. The terms HA-MRSA (healthcare-associated or hospital-acquired MRSA), CA-MRSA (community-associated MRSA) and LA-MRSA (livestock-associated) reflect this distinction.[6]

The initial presentation of MRSA is small red bumps that resemble pimples, spider bites, or boils; they may be accompanied by fever and, occasionally, rashes. Within a few days, the bumps become larger ++and more painful; they eventually open into deep, pus-filled boils. About 75 percent of CA-MRSA infections are localized to skin and soft tissue and usually can be treated effectively.[7]

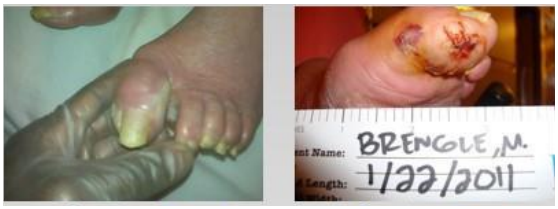
<u>MRSA Case Study 1:</u>

Patient: 71 year old female with Type II diabetes for over 10 years presented with an infected right big toe which tested positive for MRSA. Patient had been on IV Vancomycin for 6 weeks without any response. Patient was then referred to Dr. Otiko. Vancomycin was discontinued

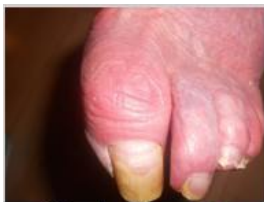
Regimen: Two drops to the wound three times daily and covered with a non-sterile dry dressing.

Result: Wound completely healed within 32 days. Skin appeared healthier than non-treated skin. Typical healing cycle: 3-4 months. In this case patient had no response with IV Vancomycin (a last resort medication, $500/day for 6 weeks, with only 40% success rate).

Before Treatment (Days 1 & 2)



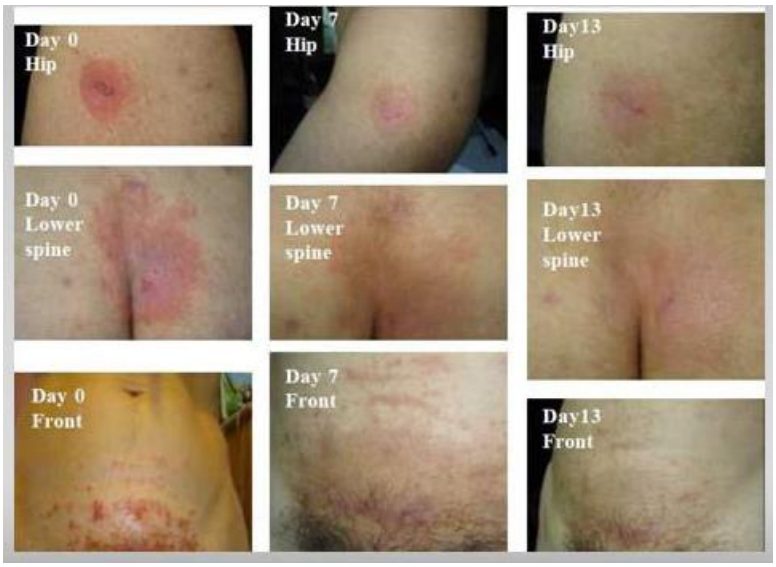
After 22 Days of Treatment



MRSA Case Study 2:

Patient: MRSA on hip, lower spine, and above pelvic area.

Result: MRSA responded to treatment within 7 days and was healed in 13 days.

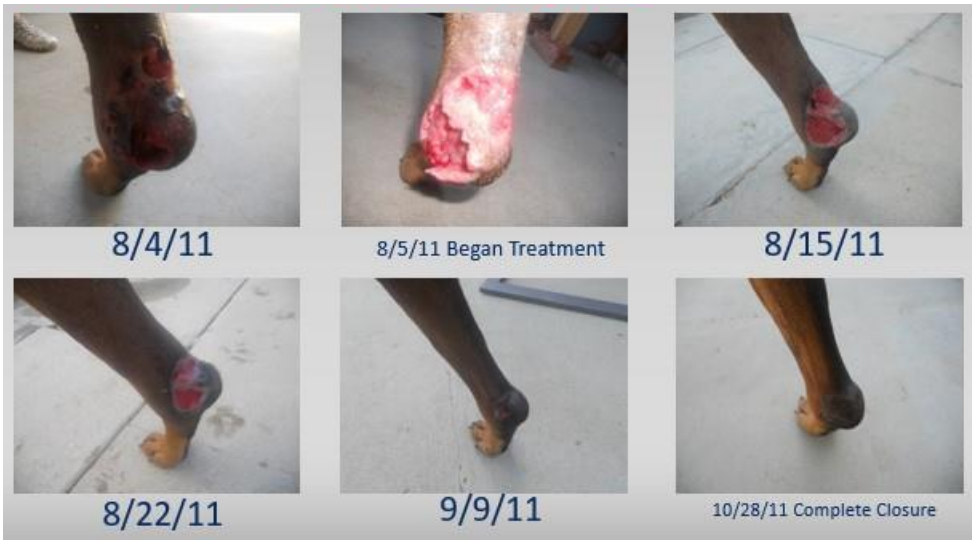


MRSA Case Study 3:

Patient: Canine patient, breed Doberman Pinscher, with a case of MRSA. Canine was scheduled to be euthanized, but owners opted to try treatment.

Result: Canine patient was completely healed in less than 2 months after treatment.

Before and After Treatment



Diabetic Foot Ulcer

A diabetic foot ulcer is an open sore or wound that most commonly occurs on the bottom of the foot in approximately 15 percent of patients with diabetes. Of those who develop a foot ulcer, six percent will be hospitalized due to infection or other ulcer-related complication.[8,9]

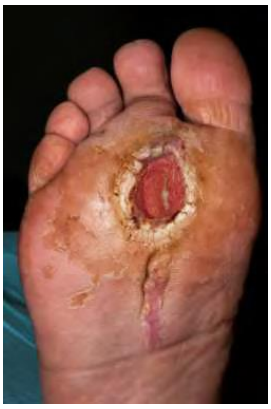
Diabetes is the leading cause of non-traumatic lower extremity amputations in the United States, and approximately 14 to 24 percent of patients with diabetes who develop a foot ulcer have an amputation.[10] As of 2015, an estimated 415 million people had diabetes worldwide.[11] As of 2014, trends suggested the rate would continue to rise.[12] The global economic cost of diabetes in 2014 was estimated to be US$612 billion.[13] In the United States, diabetes cost $245 billion in 2012.[14] With the rise of diabetes diagnoses, there is also an expected rise in the number of amputees.

<u>Diabetic Foot Ulcer Case Study 1:</u>

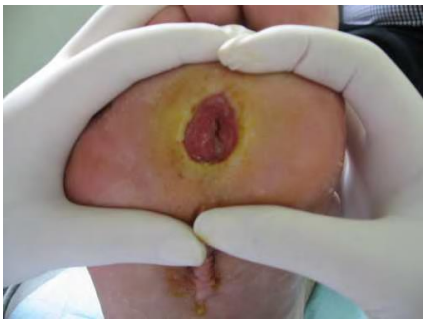
Patient: This Diabetic Foot Ulcer patient had received aggressive medical treatment for a period of time, but improvement was not forthcoming as a result of existing medical protocols. Prior to the use of Vitastem, the probability of the eventual amputation of the foot was approximately 60%.

Result: After 11 days of treatment, the lesion was healing rapidly. Granulation was proceeding, consistent with rapid healing. The vascular supply was improved, based on visual observation and the uniform color of the underlying tissue. There are no signs of infection.

Before



After 11 Days of Treatment

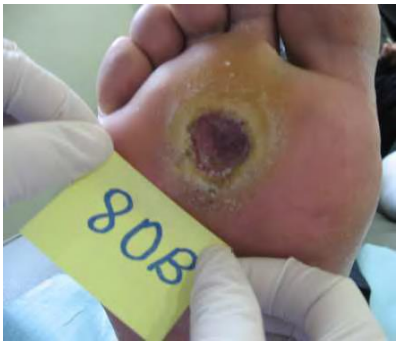


Diabetic Foot Ulcer Case Study 2:

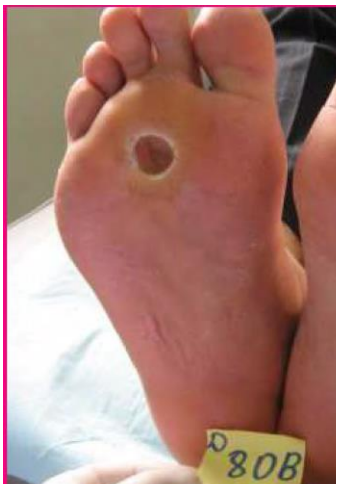
Patient: This Diabetic Foot Ulcer patient had received aggressive medical treatment for a period of time, but improvement was not forthcoming as a result of existing medical protocols. Symptoms of subcutaneous layers of muscle, poor vascular supply areas, and necrotic tissue were present.

Result: After 7 days of treatment, the lesion was healing rapidly. Granulation was proceeding consistent with rapid healing. The vascular supply was improved, based on visual observation and the uniform color of the underlying tissue. There are no signs of infection.

Before:



After 7 Days of Treatment



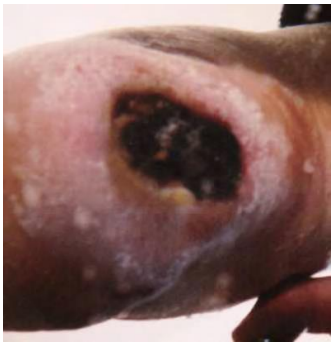
Diabetic Foot Ulcer Case Study 3:

Patient: Male, age 83, was diagnosed as a diabetic more than 5 years ago and has been under the care of physicians since that time. He began to develop foot ulcers in 2010. His left big toe was amputated in September, 2010; and the second toe on the left foot was amputated in December 2010. He developed a lesion on his right heel; it became worse; showed no signs of healing, and became infected. His physician recommended amputation of the foot in the spring of 2011.

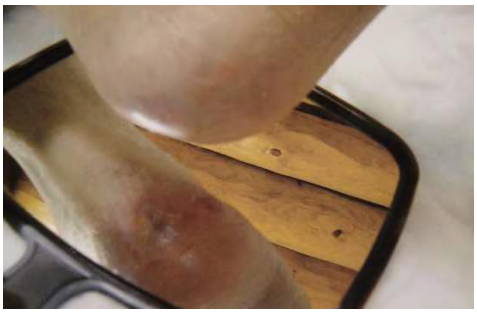
Regimen: Vitastem treatment began on June 14, 2011; once per day, applied topically.

Result: Patient began to observe improvements within 3 days after beginning the use of Vitastem. After 3 weeks, most of the tissue on the heel surrounding the lesion also showed signs of improved blood flow.

Before:



After 4 Months of Treatment



Additional Benefits for the Skin

In addition to carrying tetracycline in high concentrations across cell membranes, Vitastem also contains Dimethyl sulfoxide (DMSO), Cholcalciferol (Vitamin D3) and Ascorbic Acid (Vitamin C) which are known to have profound skin healing and regenerative effects. These ingredients are similarly carried across cell membranes by VTC technology, leading to enhanced penetration and concentration.

Dimethyl sulfoxide (DMSO)

DMSO improves blood flow and increases skin hydration by attracting water molecules. It increases tissue perfusion (the passage of fluid through tissue).[15] Despite the product containing DMSO, there is no concern for those with a Sulfa allergy due to the low concentration and non-systemic effect.[16]

Vitamin D

Vitamin D plays a crucial role in skin immunity, skin barrier function, wound healing, tissue repair, and other cellular functions in the sebaceous glands and hair follicle. Vitamin D has been shown to repair skin damage, prevent infections after skin injuries, and rejuvenate the skin. It contains strong anti-inflammatory properties that make it effective for treating burns, skin injuries and skin damage.[17]

Vitamin D is a fat-soluble prohormone steroid that has endocrine, paracrine and autocrine functions. These potential effects include inhibition of cell proliferation, promotion of cell differentiation, and apoptosis which may in turn have roles in cancer, immunity, and many organ systems. There are only three sources of Vitamin D – sunlight, diet and vitamin D supplements. Once in the circulation, vitamin D is converted by a hepatic hydroxylase into 25-hydroxyvitamin D (25(OH)D; calcidiol). The circulating 25(OH)D level is an indicator of the vitamin D status. Studies suggest that a 25-(OH)D level as high as 75 nmol/L or higher is needed to cover all physiological functions of vitamin D and should therefore be considered optimal.[18]

Vitamin D has critical roles in regulating the skin differentiation process while inhibiting proliferation; regulating skin barrier formation which is crucial for defending the skin; inducing the innate immune response in skin as well as activating receptors that result in the killing of invasive organisms; and directing antibacterial responses by modulating gene expression. Vitamin D receptors are involved in numerous cytokine and immune responses (eg. B cells, T helper cells, Regulatory T cells aka Tregs). The ability to mount an appropriate response to infection is therefore highly dependent on the availability of Vitamin D.[19]

Studies have also demonstrated that Vitamin D plays a vital role in the maintenance of the hair follicle and cellular functions in sebaceous glands, as well as having a photoprotective effect against the damage caused by UV light - which leads to DNA damage, inflammatory responses, skin cell apoptosis (programmed cell death), skin aging and skin cancer.[Error! Bookmark not defined.]

Vitamin C

Vitamin C (ascorbic acid) has numerous skin benefits. It promotes collagen synthesis, accelerates skin healing, reduces skin discoloration, evens skin tone, improves hydration, and reduces inflammation. As an antioxidant, it protects skin from sun damage and effects of pollution.[20]

Conclusion

Vitastem is an FDA registered* OTC drug and includes one of the world's strongest topical antibiotics, tetracycline. Each gram contains the active ingredient Tetracycline Hydrochloride 30mg, methylparaben, sodium hydroxide, sorbic acid, steric acid, water.

Vitastem kills all harmful bacteria that have been available for testing and that associated with conditions such as: eczema, psoriasis, acne, wounds, cuts, scrapes, and others. All known antibiotics (other than Vitastem) primarily use what's called a chemical "mechanism of kill" whereby the antibiotic attempts to kill the bacteria slowly by applying (if topical), or absorbing (if oral) more and more of the medicine over a period of time as it is taken as prescribed. While this can be somewhat effective, it takes much longer. Unfortunately, this also allows for bacteria to evolve and develop resistance to the medicine.

Vitastem uses both a chemical and a PHYSICAL mechanism to kill and fight pathogens. The physical mechanism of kill is a key feature of Vitastem's strength. Vitastem's patent-pending, specialized combination of ingredients has hacked the delivery formula that enables medicine to be transported at 10x the strength and depth of other products in the marketplace today. This formula stimulates the cell wall such that it is up to 10x more permeable than normal, allowing for substantially more medicine to enter into the cell, overwhelming and killing the bacteria so quickly that it does not have time to adapt and develop resistance. This highly concentrated and rapid delivery of medicine to the site of need is what has Vitastem many patients seeing results in 24 hours versus 5 to 7 days (as is the case with other products that treat the same conditions).

Vitastem also contains DMSO, Vitamin C, and Vitamin D, critical for healing of skin after an infection, cut, scrape or burn. Due to the effectiveness of the patent-pending delivery system, Vitastem delivers highly concentrated amounts of this Vitamin C and Vitamin D directly to the skin cells, allowing healing to take place much faster. Vitastem is ideal for wound care, trauma, and post-surgical healing.

* Disclaimer: Most OTC drugs are not reviewed and approved by FDA, however they may be marketed if they comply with applicable regulations and policies. FDA has not evaluated whether this product complies.

Where to Buy

Our specialized, innovative combinations are available to you OTC directly from our laboratory. In this manner, we are able to monitor for the highest standards of quality. It can be purchased online at: https://www.vitastem.net/products/vitastem.

Storage and Longevity of Vitastem

Keep product refrigerated to preserve its effectiveness and color. A 15 ml bottle of Vitastem contains approximately 500 drops. Depending on the skin condition, frequency of application and the amount of the surface area covered, a 15ml bottle of Vitastem generally lasts approximately 6 months to a year. Vitastem has a shelf life of TWO years, so one bottle goes a very long way.

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