REDUCING FUNGAL SKIN INFECTIONS

Supporting Skin Health with Viniferamine® Small Molecule Technology

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VINIFERAMINE®

Small Molecule Technology Without Scientific Equal™
INTRODUCTION

Fungal skin infections are fairly common and their incidence is rising due to the increasing prevalence of risk factors associated with these infections including obesity. More than 600 different fungi are reported to infect humans in various ways including skin infections. The most common human fungal pathogens are Candida species that colonize 30-50% of individuals. They are the fourth largest cause of hospital-acquired infections with Candida albicans (C. albicans) being the most common opportunistic human fungal pathogen, involved in more than 50% of all superficial Candida infections. Although C. albicans typically causes superficial skin infections and rashes, it can also cause more serious invasive infections following trauma such as surgery or extensive skin burns.

C. albicans infections are divided into four separate types: colonization (asymptomatic), superficial infections, deep seated infections and systemic infections. In healthy individuals, superficial infections of the skin occur due to a combination of skin barrier deficiency and the opportunistic growth of C. albicans, which is a common component of normal skin flora that is kept in check by other skin microorganisms. Besides obesity, factors that increase the risk of skin infection by C. albicans (cutaneous candidiasis) include antibiotic use or immunosuppression caused by stress, infections such as with HIV, cancer, diabetes, steroid therapy, or chemotherapy.

The clinical presentation of cutaneous candidiasis is variable but typically includes erythema (redness), vesicles or pimple-like bumps, and scaling with symptoms such as odor, pruritus (itching) or burning. Some rashes are fairly painful. Common areas of infection include skin folds, genital areas, buttocks, and under arms and breasts. Predisposing environmental factors include humidity, excessive sweating, and moist environments. Many of the symptoms of candidiasis including erythema and pruritus are due to an inflammatory response evoked by C. albicans infection. Effective treatment of the inflammatory component of cutaneous candidiasis is critical. Acute pruritus can result in chronic conditions and persistent scratching that may lead to the development of secondary infections.
SKIN DAMAGE, INFLAMMATION AND IMMUNE RESPONSES DUE TO CUTANEOUS CANDIDIASIS

Three stages of the infectious process are found with *C. albicans*: adhesion, invasion and damage\(^3,9\). Invasion of skin layers by the fungus is associated with its ability to switch from the yeast form to a hyphae form\(^9\). Active penetration of epithelial cells by hyphae is the major process of *C. albicans* entry into skin, which involves the destruction of keratinous layers of skin by the enzyme keratinase that is secreted by this fungus. At this stage or earlier, fungal cell surface molecules (antigens) such as mannan, glucan, and chitin stimulate immune responses including pro-inflammatory cytokine production and increased recognition by various immune cells including mast cells that respond by degranulating and attracting neutrophils\(^3,11,12\). Recently, epithelial cells and melanocytes were also both shown to be involved with the recognition of *C. albicans* as well as immune responses to *C. albicans*\(^13,14\).

THE SKIN MICROBIOME, pH AND C. ALBICANS BIOFILM FORMATION

Skin provides a fairly inhospitable environment for most microbes due to its ability to remain cool, dry and slightly acidic. The normal pH of skin ranges between 4.0 and 5.5\(^15\). Maintaining this pH range in skin is critical for the maintenance of a healthy skin microbiome. The normal skin microbiome is composed of a rich and complex flora of interacting microbes that live in harmony with skin, protecting it from potentially dangerous pathogens like *C. albicans*. Shifts in pH enable *C. albicans* to overgrow and cause skin infections including those associated with incontinence-associated dermatitis\(^4,6,10\).

Some invading microbes including *C. albicans* can resist immune responses and antibiotics (including certain antifungals) due to their ability to produce biofilms\(^10,16\). Biofilms are aggregates of microorganisms enclosed in a protective matrix that strongly adhere to surfaces including skin tissues. Many biofilms contribute to the persistence of chronic wounds\(^17\). *C. albicans* produces highly structured biofilms composed of several cell types. Like many other biofilm cells, stationary
C. albicans cells display characteristics that are very different from their free-living counterparts including the ability to produce signaling molecules that allow them to act as a multicellular entity.

SUPPORTING SKIN HEALTH WITH VINIFERAMINE® SMALL MOLECULE TECHNOLOGY

A consistent care regimen is essential for reducing fungal skin infections, particularly those caused by C. albicans. Viniferamine®, a comprehensive pH balanced skin and wound care line, contains beneficial ingredients including vital skin nutrients to help reduce inflammation, strengthen the skin barrier and provide antifungal activity.

MORE ABOUT HOW VINIFERAMINE® CAN HELP

Viniferamine® skin care products can help reduce dermatitis caused by fungal infections and can help strengthen the skin barrier to prevent fungal infections such as those caused by C. albicans. The Viniferamine® At Home™ products are designed for use in caring for skin in the comfort of the home, where healing happens.

Individuals with compromised skin due to fungal infections such as candidiasis can easily apply the products to help eliminate fungi and soothe irritations caused by fungal infections. The Viniferamine® skin and wound care products contain small molecule skin nutrients including antioxidants, vitamins and amino acids that decrease inflammation and inhibit fungi for individuals with fungal infections, as well as strengthen the skin barrier to help prevent fungal infections. Certified organic and pharmaceutical-grade ingredients in Viniferamine® products ensure that pesticides and contaminants are excluded. In fact, Viniferamine® skin and wound care products are non-sensitizing and non-irritating.
VINIFERAMINE® INGREDIENTS DECREASE INFLAMMATION AND PRURITUS

Many of the small molecule nutrients found in the Viniferamine® skin and wound care products decrease inflammation. Viniferamine® ingredient anti-inflammatory activities have been shown for the important polyphenols oleuropein, resveratrol, and EGCG (from olives, grapes and green tea respectively), as well as the important small molecules, melatonin, and L-glutathione\(^ {18-22}\). In addition, oleuropein has been shown to inhibit mast cell degranulation\(^ {23}\). Dipotassium glycyrrhizinate from licorice, avenanthramides from oats, aloe vera and shea butter were also discovered to possess anti-inflammatory activities\(^ {24-27}\).

Pruritus, or itching, is associated with inflammation and frequently evokes a scratch response. Typically, skin infected with \(C.\ \textit{albicans}\) and other fungi can be quite pruritic, however, scratching skin compromised by candidiasis can lead to secondary infections or even more invasive \(C.\ \textit{albicans}\) infections\(^ {3}\). Therefore, it is critical to decrease inflammation and pruritus associated with fungal infections. Viniferamine® anti-inflammatory ingredients can help reduce pruritus and the risk of serious complications due to pruritus caused by fungal infections.

VINIFERAMINE® INGREDIENTS HELP MAINTAIN PROPER SKIN \(\text{pH}\) AND HELP STRENGTHEN THE SKIN BARRIER

Maintaining the slight acidity of skin helps the skin maintain a healthy microbiome or community of microbes due to the fact that many pathogens prefer a higher \(\text{pH}\)\(^ {25}\). Changes in skin \(\text{pH}\) alter the normally protective microbiome and allow fungi like \(C.\ \textit{albicans}\) to invade the skin. Viniferamine® ingredients and products are \(\text{pH}\) balanced to help maintain the skin's natural \(\text{pH}\) and to ensure that the most fragile skin is free from irritation.

Viniferamine® skin care products also include ingredients that strengthen skin and improve the skin barrier to help prevent fungal infections. Quantitating transepidermal water loss (TEWL) is a way to assess the quality of the skin barrier.
and how well it functions. Oleuropein has been shown to reduce TEWL, indicating its ability to increase skin barrier function\textsuperscript{29}. Evidence also demonstrates that melatonin has a stimulatory role in building and maintaining the epidermal barrier\textsuperscript{30}.

**VINIFERAMINE® INGREDIENTS AND MICONAZOLE HAVE ANTIFUNGAL ACTIVITY INCLUDING ACTIVITY AGAINST BIOFILMS**

Miconazole has a long-standing history of successful use against fungal infections. Topical miconazole is well tolerated and has the added advantage of delivering the active compound to the desired area without systemic effects that oral antifungal medications have. The main activity of miconazole against fungi including *C. albicans* is the induction of a massive disruption of fungal cell membrane permeability resulting in the leakage of nutrients and proteins from fungal cells. Miconazole also inhibits ergosterol production that is necessary for fungal cell wall synthesis. Furthermore, miconazole inhibits various fungus-specific membrane-bound enzymes as well as fungus-specific lipid biosynthesis and inhibits *C. albicans* biofilm formation\textsuperscript{31-33}.

The Viniferamine® small molecule polyphenol ingredients oleuropein, resveratrol and EGCG all have antifungal activities including activities against *C. albicans*. In one study, an olive leaf extract with oleuropein as its major component exhibited anti-fungal activity against *C. albicans*\textsuperscript{34}. Other studies have demonstrated that resveratrol has inhibitory as well as fungicidal activity against *C. albicans*, including the induction of apoptosis (programmed cell death)\textsuperscript{35-38}. EGCG has been shown to inhibit the growth of *C. albicans* including biofilm formation\textsuperscript{39,40}. In addition, EGCG has been found to synergistically enhance the antifungal effects of miconazole including activity against *C. albicans* biofilms\textsuperscript{41}. Further, oat extract found in Viniferamine® Antifungal Skin Cream includes avenanthramides that have antifungal activities\textsuperscript{42}.
VINIFERAMINE® OFFERS AN AT HOME™ ANTIFUNGAL SKIN CARE KIT TO HELP INDIVIDUALS WITH FUNGAL INFECTIONS TAKE CARE OF THEIR SKIN IN THE COMFORT OF THEIR HOMES

The Viniferamine® Antifungal Skin Care Kit includes two highly beneficial products: Antifungal Skin Cream and Antiseptic Skin Cleanser-CS, as well as an Antifungal Skin Care Booklet written by healthcare professionals to help individuals with fungal infections take care of their skin. Viniferamine® Antifungal Skin Cream provides the proven effectiveness of 2% miconazole nitrate in a soothing petrolatum-free base. Viniferamine® Antiseptic Skin Cleanser-CS is a non-aerosol cleanser that provides continuous spray from any angle. Viniferamine® Antiseptic Skin Cleanser-CS was designed to reduce the over-population of microorganisms while maintaining the balance of the skin’s normal chemistry and flora.

SUMMARY

In summary, antifungal infections frequently involve inflammation, pruritus and weakening of the skin barrier. Viniferamine® skin and wound care products include beneficial ingredients to help individuals with fungal infections decrease inflammation and pruritus, as well as help nourish their skin to strengthen the skin barrier and aid in the recovery process. The Viniferamine® Antifungal Skin Care Kit was created for individuals with fungal infections such as cutaneous candidiasis to help them eliminate fungi and prevent further fungal skin infections.
REFERENCES


