

Undecylenic Acid

Introduction

Most organic fatty acids are fungicidal and have been used for centuries as antimicrobial agents, originally in the manufacture of soaps. In the last 50 years, however, they have found use both *in vitro* as yeast and mold inhibitors in food stuffs, and as topical and systemic antifungals. Undecylenic acid (10-



undecenoic acid) is an eleven-carbon monounsaturated fatty acid, $\text{C}_{11}\text{H}_{20}\text{O}_2$. A substance found naturally in the body (occurring in sweat), undecylenic acid is produced commercially by the vacuum distillation of castor bean oil, via the pyrolysis of ricinoleic acid. It is an economical antifungal agent and is the active ingredient in many topical over-the-counter antifungal preparations.¹ Undecylenic acid has been shown to be

approximately six times more effective as an antifungal than caprylic acid, and is effective in maintaining a healthy balance of intestinal and vaginal flora.²

Biochemistry and Pharmacokinetics

Wyss et al demonstrated more than 50 years ago that the greater the number of carbon atoms in the fatty acid chain, the greater the fungicidal activity, up to the point exceeding eleven carbon atoms, where solubility becomes the limiting factor.³

Although the fungistatic and fungicidal effects of fatty acids have been well documented, they can be somewhat irritating to mucous membranes in certain people, and commonly used fatty acids such as caprylic and undecylenic acids have an objectionable taste and odor. Consequently, the calcium, magnesium, and sodium salts of these fatty acids have been offered as reasonable alternatives. Undecylenate salts have been shown to possess as much as four times the fungicidal effect of undecylenic acid, and may be over 30 times more effective than caprylic acid.⁴ Unfortunately, the antifungal effects of these fatty acid salts are more sensitive to pH than the free fatty acids. When tested over a pH range from 4.5 to 6.0, the antifungal activities of both undecylenic acid and calcium undecylenate are quite pronounced; the minimal inhibitory concentration of calcium undecylenate against *Candida albicans* is 200 ppm at pH 6.0. However, above pH 6.0, the calcium salt is less active than the free acid, perhaps due to the suppression of ionization of the salt at higher pH levels.⁵

Alkaline pH levels in the intestinal tract are known to be caused by intestinal flora imbalance, especially by *C. albicans*.⁶ Therefore, for fatty acid salts to be effective *in vivo*, they must be delivered to the site of fungal overgrowth in the intestinal tract at an acid pH, thus avoiding both the release of excess bicarbonate from the pancreas (which would alkalize the pH) and damage to the sensitive intestinal mucosa.⁷ This can most efficiently be accomplished with a nominal amount of a substance in a time-release form, such as betaine HCl, that gradually liberates small quantities of the acid throughout the intestinal tract, simultaneously releasing the fatty acid salt.

Mechanism of Action

Undecylenic acid has long been known to have anti-fungal properties. At least one of the mechanisms underlying its anti-fungal effect is its inhibition of morphogenesis of *Candida albicans*. In a study on denture liners, undecylenic acid in the liners was found to inhibit conversion of yeast to the hyphal form.⁸ Hyphae were associated with active infection. The authors speculated on possible mechanisms including interference with fatty acid biosynthesis, which can inhibit germ tube (hyphae) formation. Medium-chain fatty acids have also been shown to disrupt the pH of the cell cytoplasm by being proton carriers.⁹

Clinical Indications

Vaginal/Gastrointestinal Candidiasis

Undecylenic acid has been shown to be effective in preventing fungal overgrowth associated with vaginal and gastrointestinal candidiasis via its fungicidal activity. A study published in the *Journal of the American Medical Association* found a direct correlation between vaginal yeast infections and simultaneous overgrowth of *Candida* in the digestive tract.¹⁰ Undecylenic acid has long been known to be fungicidal against *Candida albicans*, thus helping achieve a healthy balance of normal vaginal and intestinal flora.²

Thrush

Since undecylenic acid acts systemically, oral administration can inhibit or even prevent oral candidiasis, or thrush. While large-scale clinical studies have not been conducted, many case reports confirm undecylenic acid's efficacy in thrush. During lactation, oral administration of undecylenic acid to nursing mothers can prevent thrush in babies. The milk, however, may taste slightly different to the infant.

Dermatomycoses

Undecylenic acid is the active ingredient in Desinex® cream and a number of other over-the-counter antifungals. It is responsible for the antifungal effect of these medications against such organisms as *Candida albicans*, *Trichophyton*

species, *Epidermophyton inguinale*, and *Microsporum audouini*.¹

A double-blind study of 151 patients with tinea pedis demonstrated that a powder containing 2-percent undecylenic acid and 20-percent zinc undecylenate resulted in a remarkable decrease in infection rate and symptomology, when compared to patients given a placebo powder. Eighty-five patients, who were culture positive for *Trichophyton rubrum* or *Trichophyton mentagrophytes*, were assigned to receive the active powder, and of these, 88 percent had negative cultures after four weeks, compared to 17 percent of those treated with placebo powder. There were no side effects or adverse reactions to the powder containing undecylenic acid and its zinc salt.⁵

Herpes Simplex Infection

Undecylenic acid has been shown to have antibacterial and antiviral properties *in vitro* and is effective topically against the herpes simplex virus in both animals and humans. Two studies, one using a 20-percent solution¹¹ and the other a 15-percent cream,¹² demonstrated a decrease in the incidence and duration of viral shedding in subjects inoculated with herpes simplex virus. Patients also experienced a significant decrease in pain and tenderness at the lesion site. The antiviral activity was, however, of relatively short duration and most pronounced when undecylenic acid was applied during the prodromal stage of outbreak. Slight local skin irritation and dysgeusia (altered sense of taste) were experienced by some subjects.^{9,10}

Denture Stomatitis

Candida albicans is a major cause of denture stomatitis, an inflammation of the tissues underlying dentures. The organism exists in two cellular morphologies – the round yeast form found in asymptomatic carrier states and the branching hyphal form found in active infections. Resilient liners are frequently used to treat denture stomatitis, and McLain et al demonstrated that liners containing undecylenic acid completely inhibited the conversion of the yeast form of *Candida albicans* to the hyphal form, thereby inhibiting proliferation of the yeast.⁸

Safety/Toxicity

Relatively small doses of undecylenic acid and its salts have been shown to have powerful antifungal properties, and the dosages necessary to achieve therapeutic benefit appear to be safe. Capsules or gelcaps of undecylenic acid should not be opened and mixed with food or drink as the taste and odor is objectionable and it may also be irritating to mucous membranes. Additionally, undecylenic acid in an oil base should not be applied directly to the skin, unless diluted in olive oil, as it may otherwise result in skin irritation.

Dosage

Undecylenic acid given orally is typically in an oil-based gelcap or as powder (in the case of its salts) in a two-part capsule. Adult dosage is usually 450-750 mg undecylenic acid daily in three divided doses.

References

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