

CYTOCHROME P450

OR WHAT'S IN A NAME...

The metabolism of fungi is almost identical to that of other eukaryotic organisms, such as humans. Therefore, trying to design a systemic drug that kills fungi without harming their human host means searching for infinitesimal differences in metabolic pathways.

Selective precision for the metabolic pathways in fungi, as distinct from those in humans, remains the key determinant for any systemic antimycotic, regardless of its point of biochemical interaction. This precision has been achieved to an exceptional degree with itraconazole, alias Sporanox*, because it selectively inactivates the fungal cytochrome P450 only.

Figure 1 is a simplified illustration of one of the pathways for the enzymatic ergosterol synthesis in fungal cell membranes. (Ergosterol is essential for the structural cohesion of these membranes). Pharmacologically one can disrupt this process at two distinct points. The first is where squalene is made into an oxide. Alternatively, one can interfere where lanosterol is converted into ergosterol, by inactivating **cytochrome P450** — a chemical catalyst that performs a vital function in the enzymatic reaction. The broadest research experience to date has been gathered with the latter approach. Importantly, in view of the close similarities between the enzymatic processes in fungi and humans, either approach must be highly selective in disrupting the fungal enzyme systems only.

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SHORT AND SIMPLE ORAL THERAPY

standard dose in dermatomycoses: 1 capsule (100 mg) once daily for 14 days
standard dose in vaginal candidosis: 2 x 2 capsules (400 mg) for 14 days

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Properties: Sporanox (itraconazole), a triazole derivative, is orally active against infections with dermatophytes (*Trichophyton* spp., *Microsporum* spp., *Epidermophyton floccosum*), yeasts (*Candida* spp., *Pityrosporum* spp.), *Aspergillus* spp. and various other yeasts and fungi. **Indications:** Sporanox (itraconazole) is indicated for vulvovaginal candidosis, pityriasis versicolor, dermatophyoses, fungal keratitis and oral candidosis. **Dosage and administration:** Vulvovaginal candidosis: 2 capsules (200 mg) morning and evening for 1 day. Pi-

tyasis versicolor: 2 capsules (200 mg) once daily for 7 days. - Tinea corporis, tinea cruris, tinea pedis, tinea manus: 1 capsule (100 mg) daily for 15 days; highly keratinized regions, as in plantar tinea pedis and palmar tinea manus, require 1 capsule (100 mg) daily for 30 days. - Oral candidosis: 1 capsule (100 mg) daily for 15 days. - Fungal keratitis: 2 capsules (200 mg) once daily for 21 days. **Contra-indications:** Sporanox (itraconazole) is contra-indicated during pregnancy. **Warnings:** **Precautions:** Although clinically **Sporanox** appears to be safe, it should be used with caution in patients with a history of liver disease.

zole) has not been established, it is advisable not to give it in known history of liver disease, recent history of alcohol abuse, or hypertension.

DRAFTING

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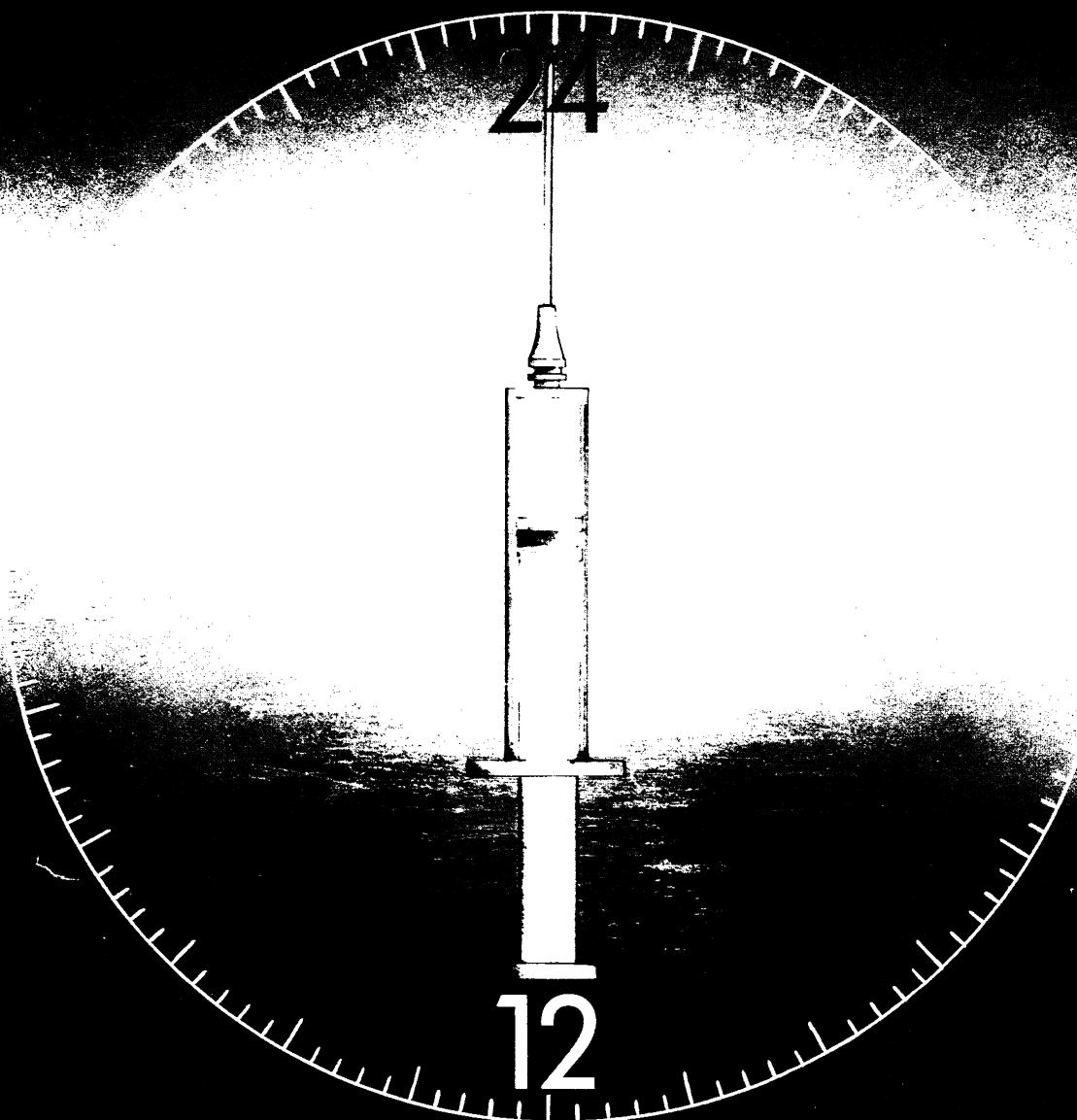
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