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## SHORT REPORT

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### A PRELIMINARY STUDY ON THE ANTIFUNGAL ACTIVITY OF 2,4,3',5'-TETRAHYDROXYSTILBENE ON DERMATOPHYTES

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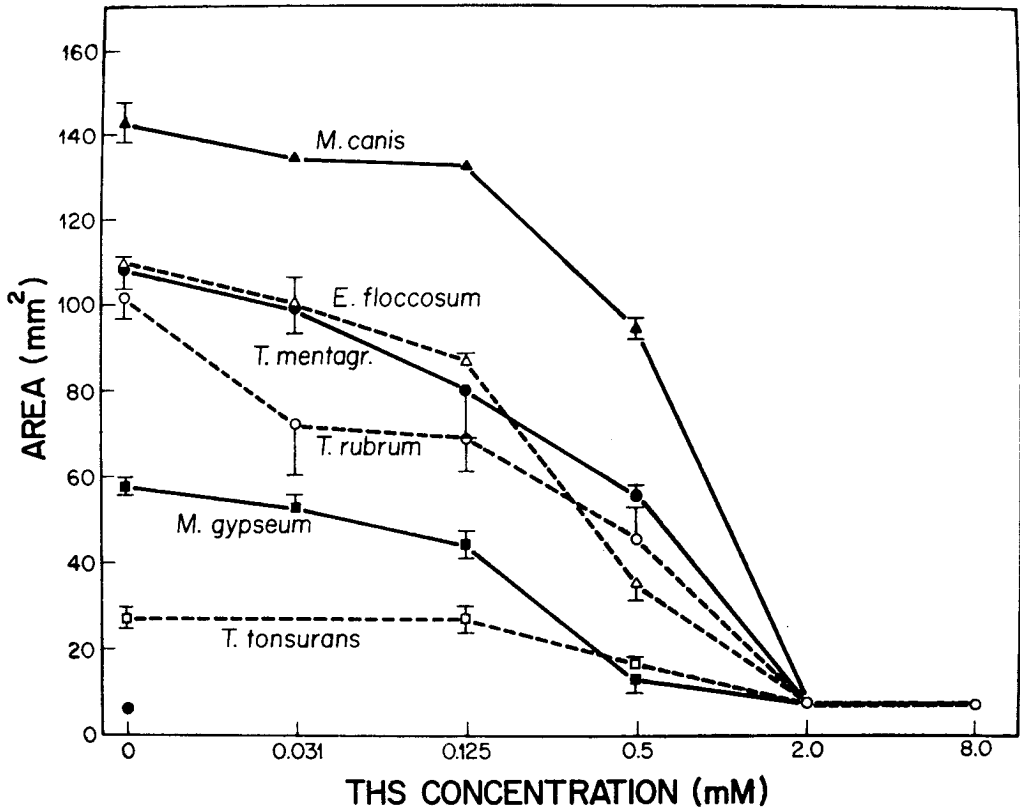
#### Summary

*2,4,3',5'-Tetrahydroxystilbene has been shown to inhibit the growth of Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans, Microsporium canis, Microsporium gypseum and Epidermophyton floccosum. The minimal inhibitory concentration was 2.0 mM in all cases. It is inactive against Candida albicans.*

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2,4,3',5'-Tetrahydroxystilbene (THS) is a phenolic compound isolated from the aqueous extract of *Artocarpus lakoocha* Roxb. heartwood<sup>1</sup>. The substance was first isolated by Takaoka<sup>2</sup> from the root of the white hellebore (*Veratrum grandiflorum*) and from Osage orange (*Toxylon pomiferum*). THS and other hydroxystilbene derivatives from these plants have attracted attention because of their fungicidal and fungistatic properties on wood-destroying fungi<sup>3</sup>. Barnes and Gerber<sup>4</sup> showed that THS is responsible for antifungal action of the aqueous extract of Osage orange wood and that it inhibits the growth of five out of thirteen fungi tested. It has been suggested that the remarkable resistance of certain woods for example, Osage orange and *Artocarpus lakoocha* Roxb. is due to the toxicity of THS on the fungi which normally initiate the decomposition process. Moreover, the aqueous extract of *Artocarpus lakoocha* which contain up to 70% THS has been used in Thailand as anthelmintic<sup>5</sup> and antipruritic<sup>6</sup>. Recently it has been shown that THS exhibits interesting actions on the oxidative phosphorylation by rat liver mitochondria<sup>7</sup>.

In view of the antifungal activity of THS studied mostly on wood-destroying fungi and the claimed antipruritic property of the *Artocarpus lakoocha* extract it is of interest to see whether THS (purified as described in ref. 1) exerts inhibitory action on dermatophytic fungi normally responsible for topical fungal infections.



**Fig. 1.** The areas of the fungal colonies as a function of THS concentration. The dermatophytic fungi were grown on Sabouraud dextrose agar in the absence and presence of THS at the indicated concentrations for 5 days at 28°. Each point represents the mean of 6 observations  $\pm$  SE. The colony size at time zero is shown at the lower left corner.

The dermatophytes used in the present study include *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Microsporum canis*, *Microsporum gypseum* and *Epidermophyton floccosum*. In addition, *Candida albicans* was studied. They were isolated from patients of The Institute of Dermatology, Bangkok, and were used within two weeks after isolations and identifications. These fungi except *C. albicans* were first grown on Sabouraud dextrose agar and small circular discs (diameter 2 mm) of the fungi were placed on solid media containing various concentrations of THS. In the case of *C. albicans*, the yeast was streaked on the THS-incorporated agar plates. The following final concentrations of THS were used: 0.031, 0.125, 0.5, 2.0 and 8.0 mM. The fungi were then allowed to grow at 28° for 5 days. The average diameters of the colonies were measured with the use of a calibrated magnifier. The results, expressed in terms of areas of the colonies as a function of THS concentrations, are shown in Fig. 1. The logarithmic abscissa in Fig. 1. was employed merely as a convenience in presenting the data and does not imply an inverse exponential relationship between the area and THS concentration. It is clear that THS inhibits the growth of all six fungi tested. The minimal inhibitory concentration (MIC) of THS in all cases under these conditions was 2.0 mM. *Candida albicans* was insensitive to THS even at 8.0 mM.

The fungi that have been shown to be sensitive to THS in the present study together constitute 98.97% of the fungi responsible for superficial dermatomycosis found in Bangkok. This figure is based on the data obtained by Kotrajaras and Chongsathien<sup>8</sup> at the Institute of Dermatology in 1975. They showed that *T. rubrum*, *T. mentagrophytes*, *E. floccosum*, *M. gypseum*, *T. tonsurans* and *M. canis* were responsible for 67.20%, 19.67%, 9.38%, 1.41%, 0.81% and 0.50%, respectively, of the 991 cases of superficial dermatomycosis seen at the Institute.

As mentioned earlier, the extract of *Artocarpus lakoocha* has been used in Thai traditional medicine as an antipruritic. The observation that THS which is the main component of the plant extract inhibits the growth of these fungi may constitute a pharmacological basis for the claimed antipruritic activity

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### บทคัดย่อ

ได้พบว่า 2,4,3',5'-tetrahydroxystilbene ยับยั้งการเจริญเติบโตของ *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Microsporum canis*, *Microsporum gypseum* และ *Epidermophyton floccosum* ความเข้มข้นต่ำสุดที่จะยับยั้ง คือ 2.0 mM ในทุกชนิด สารนี้ไม่ยับยั้งการเจริญเติบโตของ *Candida albicans*