

## Study of Cytotoxic Activity of Neolignans 8.O.4', Arylpropanoids and Related Compounds with Antifungal Properties

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**SUMMARY.** The cytotoxic effects of neolignans 8.O.4', arylpropanoids and structurally related compounds are reported. Compounds having a strong antifungal activity, in parallel possess a potent cytotoxic effect, very similar to those displayed by amphotericin B and ketoconazole. Our results indicate that the actual role of arylpropanoids acting as antifungal compounds could be limited for topical use. However the strong antifungal activity and the novel mechanism of action of these arylpropanoids open the possibility of a promising utilization in agriculture and veterinary.

**RESUMEN.** "Estudio de la Actividad Citotóxica de Neolignanos 8.O.4', Arilpropanoides y Compuestos Relacionados con Propiedades Antifúngicas". Se reportan las actividades citotóxicas de neolignanos del tipo 8.O.4', arilpropanoides y compuestos estructuralmente relacionados. Aquellos compuestos que poseen una fuerte actividad antifúngica presentaron paralelamente una importante actividad citotóxica, ambas comparables a las que mostraron anfotericina B y ketoconazol. Nuestros resultados indican que el verdadero rol de los arilpropanoides actuando como compuestos antifúngicos podría estar limitado a un uso tópico. La fuerte actividad antifúngica y el novedoso mecanismo de acción de estos fenilpropanoides abren la posibilidad de una promosoria utilización en agricultura y veterinaria.

### INTRODUCTION

The development of efficacious antifungal agents has not been as successful as that of antibacterial agents. The main reason is that fungi and mammals are both eukaryotes and their metabolic pathways are not significantly different. Consequently, it is difficult to develop new selective antifungal agents. However, the need for new antifungal agents is due to the increase of fungal infections in particular in immunocompromised hosts<sup>1</sup>.

There is a vast literature dealing with the treatment of mycotic infections in normal and immunocompromised patients<sup>2-4</sup>. Thus, there appears to be a large and impressive array of drugs for the treatment of fungal infections. Unfortunately, the reality is quite different. There are, in fact, only very limited therapeutic options. Most of the available drugs have signifi-

cant and potentially life threatening side effects.

In the course of our screening program for antifungal activity, we report that 8.O.4' neolignans possess moderate but significant antifungal activity against dermatophytes<sup>5,6</sup>. Considering that neolignans are plants compounds formed by two C<sub>6</sub>-C<sub>3</sub> units, and dimerization of phenylpropanoids through dehydrogenation, produces the skeleton of all natural and synthetic lignans known to date, we carried out a systematic study of the antifungal properties of their phenylpropanoid moieties plus several structurally related compounds<sup>7</sup>. In that paper, we reported a strong antifungal activity of phenylpropanoids against dermatophytes. The antifungal effect of these compounds was comparable to those of amphotericin B and ketoconazole.

To gain insight into the mode of action of

**KEYWORDS:** Antifungal activity, Arylpropanoids, Cytotoxicity.

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