



# SYNERGISTIC EFFECTS OF DIPHENYL DISELENIDE AND AMPHOTERICIN B IN *Trichosporon asahii* ISOLATES



D. Alves Nunes Mario, T. Felli Kubiça, P. Orlandi Barth, E. Silva de Loreto, C. Nogueira, L. Bedin Denardi, S. Hartz Alves

Laboratory of Mycological Research, Department of Microbiology, Universidade Federal de Santa Maria, Santa Maria, RS, Brasil

debora\_alves6@hotmail.com

## 1. INTRODUCTION

Disseminated infections caused by *Trichosporon asahii* are difficult to resolve. Combination regimens with synergistic drugs could provide additional options for treating trichosporonosis.

In this context, the aim of this study was to evaluate the in vitro activity of diphenyl diselenide [(PhSe)<sub>2</sub>] alone and in combination with amphotericin B against *Trichosporon asahii* clinical isolates.

## 2. METHODS

Susceptibility tests were performed according to the CLSI protocol M27-A3 microdilution technique and the interaction between diphenyl diselenide [(PhSe)<sub>2</sub>] and amphotericin B against 10 *Trichosporon asahii* clinical isolates was evaluated using the microdilution checkerboard method. The concentrations of diphenyl diselenide [(PhSe)<sub>2</sub>] ranged from 0.5 µg/mL to 64 µg/mL, and the concentrations of the amphotericin B ranged from 0.03 µg/mL to 4 µg/mL. The fractional inhibitory concentration (FIC) was calculated for each agent by dividing the minimal inhibitory concentration (MIC) of each drug in combination by the MIC of the drug alone. The FIC values were then totaled to determine the fractional inhibitory concentration index (FICI) that resulted from the drug combinations. Synergism was defined as an FICI ≤ 0.5, indifference was defined as 0.5 < FICI ≤ 4, and antagonism was defined as FICI > 4.

## 3. RESULTS

The results of the in vitro susceptibility test, FICI and the resulting drug interactions against *Trichosporon asahii* clinical isolates are described in Table 1. MICs ranged from 8 to 64 for (PhSe)<sub>2</sub> and 1 to 4 for amphotericin B. When *T. asahii* isolates were tested for the (PhSe)<sub>2</sub> + amphotericin B synergistic interactions were observed in 100% of the isolates, whereas no antagonistic or indifferent interactions were observed.

**Table 1.** In vitro susceptibility and interactions between diphenyl diselenide [(PhSe)<sub>2</sub>] and amphotericin B (AmB) against clinical isolates of *Trichosporon asahii*.

Clinical isolates	MIC (µg/mL)		MIC (µg/mL) combination		
	AmB	(PhSe) <sub>2</sub>	AmB / (PhSe) <sub>2</sub>	FICI	Interaction
<i>T. asahii</i> 1	1	8	0.25/0.5	0.3125	Synergism
<i>T. asahii</i> 2	1	8	0.25/0.5	0.3125	Synergism
<i>T. asahii</i> 3	1	8	0.25/0.5	0.3125	Synergism
<i>T. asahii</i> 4	1	8	0.125/0.5	0.1875	Synergism
<i>T. asahii</i> 5	4	64	0.031/8	0.0703	Synergism
<i>T. asahii</i> 6	2	64	0.25/0.5	0.1328	Synergism
<i>T. asahii</i> 7	1	8	0.25/0.5	0.3125	Synergism
<i>T. asahii</i> 8	2	8	0.25/0.5	0.1875	Synergism
<i>T. asahii</i> 9	1	32	0.25/0.5	0.265	Synergism
<i>T. asahii</i> 10	4	64	0.031/8	0.0703	Synergism

## 4. CONCLUSION

In conclusion, we reported that (PhSe)<sub>2</sub> inhibited the in vitro growth of *Trichosporon asahii* isolates, and we provided a new approach to *Trichosporon asahii* susceptibility studies once the association of (PhSe)<sub>2</sub> with AmB presents a synergistic potential. New experimental in vivo protocols are needed and will promote a better understanding of (PhSe)<sub>2</sub> antimicrobial activity and its use as an adjuvant therapy with antifungal agents.