



Acute Toxicity Study of Commercial Antifungal Drugs using *Poecilia reticulata*

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SUMMARY. Commercial antifungal drugs possess important side effect; being toxicity the main limitation of such compounds. We report here a study of acute toxicity of four well-known commercial antifungal drugs; two of them used in human medicine (griseofulvine and miconazole) and the other two used against phytopatogens fungi (carbendazin and benomil). Toxic effects of these compounds were evaluated using an acute toxicity test on fish of the specie *Poecilia reticulata*.

INTRODUCTION

Commercial drugs used against pathogenic fungi and phytopatogens are toxic for many organisms ¹. This is particularly important for drugs of aerial use like antifungal agents used against phytopatogenic fungi. Recently it has been reported the presence of azoles in aquatic organisms ². On the other hand it is interesting to note that toxicity is a very important limitation for the use of any commercial antifungal drug.

We report here a comparative study of acute toxicity of four well-known commercial antifungal drugs. Two of them used in human medicine (miconazole and griseofulvine) ³ and the other two used against phytopatogenic fungi (carbendazim and benomil) ⁴.

Methodology

Toxic effect of compounds was evaluated using a toxicity test on fish. The static technique recommended by the U.S. Fish and wildlife Service Columbia National Fisheries Research Laboratory ⁵ was modified in order to use lower amounts of tested compounds ⁶. Fish of the

specie *Poecilia reticulata* were born and grown in our laboratory until they reached a size of 0.7–1.0 cm (15 days old). In the toxicity test, 10 specimens were exposed to each of the three concentration tested per drug (20, 2 and to 0.2 µg / ml) in 2 L wide-mouthed jars containing the test solutions. The test began upon initial exposure to the potentially toxic agent and continued for 96 h. The number of dead organisms in each test chamber was recorded and the dead organisms were removed every 24 h; general observations on the conditions of tested organisms were also recorded at this time; however the percentage of mortality was recorded at 96 h. Each experience was performed two times with three replicates each.

We chose this technique because it is fast, economic and easy to reproduce. This assay has been previously used by our group testing the toxicity of synthetic and natural compounds ^{6,7}. The specie *Poecilia reticulata* has been previously used in acute toxicity test ⁸.

RESULTS

Results are summarized in Table 1.

KEY WORDS: Acute toxicity, Antifungal drugs, *Poecilia reticulata*.

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Drugs	Concentration	N° Specimens		Percentage of Mortality		
		0 hs	24 h	48 h	72 h	96 hs
DMSO	0.6 ml/l	10	0	0	0	0
Miconazole	20 µg/l	10	100	-	-	100
Miconazole	2 µg/l	10	50	100	-	100
Miconazole	0.2 µg/l	10	0	0	20	20
Griseofulvine	20 µg/l	10	40	100	-	100
Griseofulvine	2 µg/l	10	0	20	40	60
Griseofulvine	0.2 µg/l	10	0	0	0	0
Carbendazim	20 µg/l	10	0	0	0	0
Benomil	20 µg/l	10	0	0	0	0
Control	-	10	0	0	0	0

Table 1. Acute toxicity obtained for the different compounds. Results are shown as percentage of mortality.

Miconazole produces 100% of mortality at 24 hs (20 µg/ml); whereas using 10 times lower concentration (2 µg/ml) it produces 100% of mortality at 48 hs. Even at low concentrations (0.2 µg/ml) this drug causes 20% of mortality at 96 hs of exposition; showing a significant acute toxicity. Griseofulvine shows a lower toxicity in comparison to miconazole, giving 100 % of mortality at 48 hs (20 µg/ml). This drug produces 40 % of mortality at 96 hs (2 µg/ml); being non toxic at 0.2 µg/ml. We also calculated the IC₅₀⁹ values for both compounds obtaining 0.2039 µg/ml and 1.9268 µg/ml for miconazole and griseofulvine, respectively.

CONCLUSIONS

It is interesting to note that for carbendazim and benomil we did not find acute toxicity against fish at the concentrations tested here. Thus, it appears that the acute toxicities displayed by miconazole and griseofulvine against the specie *Poecilia reticulata* are completely different to those observed for carbendazim and benomil. The lack of acute toxicity obtained for the latter compounds is a very important characteristic considering the aerial use of both drugs.

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