## ANTIPROLIFERATIVE ACTIVITY OF HYDRAZONES AND AJOENE ON ISOLATES OF *C. NEOFORMANS*. SYNERGIC EFFECTS

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*Cryptococcus neoformans* is the causal agent of the cryptococcosis, a systemic disease of general sub-acute or chronic course. Currently, it is used anfotericine B (AMB), fluconazol or combined doses of anfotericine B and 5-fluorocitosine (5-Fc). These anti-fungi showed variable results and undesirable side effects produced by its acting mechanism. For these reasons, possible inhibitors of 24-sterol-methyltransferase (Azasterols and Hydrazones), as well as inhibitors of phospholipid synthesis (Ajoene), have been explored. As main objective, the evaluation of sensitiveness of *Cryptococcus neoformans* isolates to inhibitors of the synthesis of polar (ajoene) and neutral lipid (hydrazones) were performed. For the susceptibility assays a micro-dilution method was used and the anti-fungi tested were: Hydrazone 1, Hydrazone 2, Hydrazone 3, Hydrazone 4 and Ajoene. Results shown dose-dependent effects and sensitivity differences between the isolates, revealed by different percentages of inhibition of each drug, Ajoene 40 to 60%, H1 40 to 75%, H2 25 to 50%, H3 35 to 85% and H4 12 to 35% and differences in calculated CMI and $CI_{50}$, CMI Ajoene 25 to 50 µM, $CI_{50}$ 4 to 12 µM; CMI H1, H2 and H3 10 µM, H4 3 to 10 µM and $CI_{50}$ all Hydras 0.3 to 4.0 µM In regard to the combination of Ajoene + Hydrazone 3, a CIF value of 0,16 was obtained, signifying a marked synergic effect observed in the corresponding isobologram with a very marked concave curve. The synergic effects obtained in the present work suggests the possibility of combined therapies with both drugs, diminishing the possible side effects and preventing or delaying the appearance of resistant isolates to one of the anti-fungi.

**Key words**: *Cryptococcus neoformans*, anti-fungi, Cryptococcosis, synergism