

TITLE: EVALUATION OF ANTIFUNGAL ACTIVITY OF THE MONOTERPENE PERILLYL ALCOHOL AND ITS ASSOCIATION WITH COMMERCIAL ANTIFUNGAL AGENTS.

AUTHORS: LUIZ, S. R. S.⁽¹⁾; SANTOS, F. C. V.⁽²⁾; BATISTA, A. D.⁽¹⁾; GOULART, F.⁽¹⁾; ALVIANO, C. S.⁽¹⁾; ALVIANO, D. S.⁽¹⁾

INSTITUTION: (1) INSTITUTO DE MICROBIOLOGIA PAULO DE GÓES (CENTRO DE CIÊNCIA DA SAÚDE, BLOCO I, CIDADE UNIVERSITÁRIA, RIO DE JANEIRO, RJ). (2) INSTITUTO DE QUÍMICA (AVENIDA ATHOS DA SILVEIRA RAMOS, BLOCO A, 7ºANDAR, CEP: 21941-909 – CENTRO DE TECNOLOGIA, CIDADE UNIVERSITÁRIA, RIO DE JANEIRO, RJ).

ABSTRACT

Perillyl alcohol (POH) is a monoterpene hydroxylated monocyclic formed by two isoprene units from the biosynthetic pathway of mevalonate. It is found in small concentrations in the essential oils of lavender, pepper, mint, cherries, celery seeds and several other plants, and can be obtained through the biotransformation of limonene or in a synthetic way. Currently in vitro and in vivo studies have shown that its main pharmacological action is as chemopreventive of colon, skin, lung and brain tumor cancer. Based on this, the search for other pharmacological activities of this monoterpene, for example, antifungal is stimulated, considering that there are few reports in the literature referring to this activity. In this context, the present study proposes to verify the antifungal activity of perillyl alcohol and its association with commercial antifungal agents. Initially the yeasts fungi tested were: *Cryptococcus neoformans* 24067 and Cap 67, *Cryptococcus gattii* 10697 and R265. The minimum inhibitory concentration (MIC) of the POH was determined based on the international standard methodology *Clinical and Laboratory Standard Institute-CLSI* M27-A3 described for yeasts, and M38-A described for filamentous fungi. The minimum microbiocidal concentration (MMC) of the POH consists of the minimum concentration capable of inhibiting the growth of colony-forming units. The evaluation of the synergistic effect will be performed through the interaction of different concentrations of the POH with the commercial antifungal agents, such as amphotericin B and fluconazole. Among all fungi tested, those that was more sensitive to POH was *Cryptococcus neoformans* 24067, which presented a MIC/MMC of 156µg/mL/625µg/mL, respectively. In association with commercial antifungal agents, only *C. neoformans* 24067 showed a synergistic effect when associated with both amphotericin B and fluconazole. Thus, the preliminary results indicate that POH is a promising substance as antifungal, mainly when associated with commercial drugs, being effective against the strain of *C. neoformans* tested in vitro.

Keywords: antifungal, *C. neoformans*, Perillyl alcohol, synergism.

Development Agency: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.