Anticandidial Effect of Phenylbutene Derivatives and Their Interaction with Ergosterol

Svoboda Tabakova[a], Iliya Manolov[b], Todor Kantardjiev[c], Grisha Mateev[d], Konstantin Stoichkov[e], Anna Braykova[a], Victoria Vakhan[a] and Evgeny Golovinsky[a]

[a] Institute of Molecular Biology, The Bulgarian Academy of Sciences, Sofia, Bulgaria
[b] Department of Organic Chemistry, Faculty of Pharmacy, Higher Medical Scholl, Sofia, Bulgaria
[c] Microbiological Department, National Centre of Infectious and Parasitic Diseases, Sofia, Bulgaria
[d] Department of Dermatology, Higher Medical School, Sofia, Bulgaria
[e] Clinic of Dermatology, National Centre of Oncology, Sofia, Bulgaria

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This paper reports the effect of phenylbut-3-en-2-one, of its analogues, bearing 3-nitro, 4-nitro, 4-chloro- and 4-dimethylamino substituents at the phenyl moiety, and of the hydrazide, phenylhydrazide and oxime of 4-nitrophenylbut-3-en-2-one on the growth and germ-tube formation of *Candida* spp., as well as their ability to interact with ergosterol in water/dimethylformamide (DMF) solution and their acute toxicity for mice. 3-Nitro-, 4-nitro- and 4-chlorophenylbut-3-en-2-ones inhibit candidial growth *in vitro* in concentrations ranging from 0.01 to >0.4 mM and their activity is comparable to that of ketoconazole (in mg/l) and lower than that of amphotericin B. The rest of the compounds are inactive at >0.4 mM. Germ-tube formation of *C.albicans* is inhibited at 0.04 mM 4-nitrophenylbut-3-en-2-one and at 0.005 mM of the 3-nitro isomer. A decrease in the absorption maxima in ergosterol mixtures with 4-dimethylamino, 3-nitrophenylbut-3-en-2-one and the oxime of the 4-nitrophenylbut-3-en-2-one was observed, indicative of interaction in water/DMF solutions, while no changes in the UV spectra of the remaining compounds were detectable. That suggests that the growth inhibiting effect is not in correlation with their ability to interact with ergosterol, despite the resemblance to polyenes. LD_{50} for mice is 367 mg/kg for 4-nitrophenylbut-3-en-2-one and 398 mg/kg for the 3-nitro isomer.

Reprint requests to Dr. Svoboda Tabakova. E-mail: svt@bas.bg