Clarification of the mechanism of action of ozonized oil eye drops in liposomes against *Candida* spp.

Pierangelo Bellio, PhD, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
Giuseppe Celenza, Professor, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

Abstract

Introduction: Ozone is commonly used as in a number of fields. The antimicrobial, antifungal and antiviral action is well known, as its ability to prevent the development of antimicrobial resistance and allergic reaction, since the product of reaction is molecular oxygen. The use of ozonized oils to treat external urogenital or wound infections is encouraged specially where the infection is sustained by MDR strains. Keratitis are often associated with fungal infections induced by filamentous fungi (*Aspergillus, Fusarium*) or yeast-like fungi (*Candida*). They are more dangerous and devastating than bacterial keratitis as the diagnosis and treatment are challenging. *C.albicans* keratitis are frequently associate with systemic illness or complicated chronic ocular diseases. We investigated the mechanism of action of ozonized oil eye drops in liposomes (ed-OZO) against clinical Candida: *C.albicans* (CA), *C.glabrata* (CG), *C.krusei* (CK) and *C.orthopsilosis* (CO).

Material and Methods: Organisms were obtained from S.Salvatore Hospital in L'Aquila. The antifungal activity of ed-OZO was evaluated using microdilution method (EUCAST-AFST) and IC_{50s} were also determines. CA membrane depolarization was investigated by fluorimetric assay using DisC3(3) in a range of ed-OZO from 1/128×MIC to 1×MIC.

Results: *Candida* spp. are susceptible to ed-OZO (vol/vol): CA, 3.125%; CG, 0.195%; CK, 0.78%; CO, 6.25%. CA membrane depolarization occurs instantaneously after exposure to ed-OZO at concentrations well below MIC value as well as dose dependent membrane depolarization. Increasing in ROS is observed at the highest ed-OZO concentrations, as well as membrane lipid peroxidation.

Discussion and Conclusion: This study evaluated the antimycotic activity and mechanism of action of ed-OZO. It shows good antimycotic activity at dilution from 32- to 512-fold against all candida species. In *C.albicans*, used as model for mechanism investigation, eye drop acts inducing alteration of membrane function and structure. The increase in ROS species and subsequent membrane lipid peroxidation might explain the strong antimycotic activity.

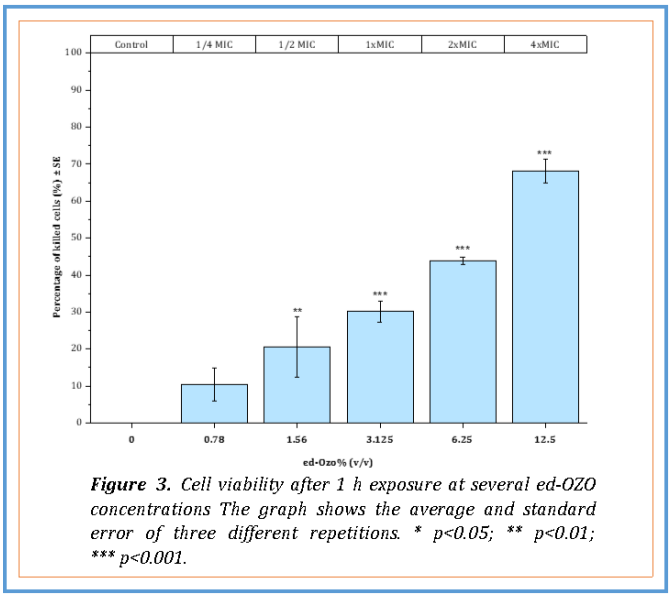
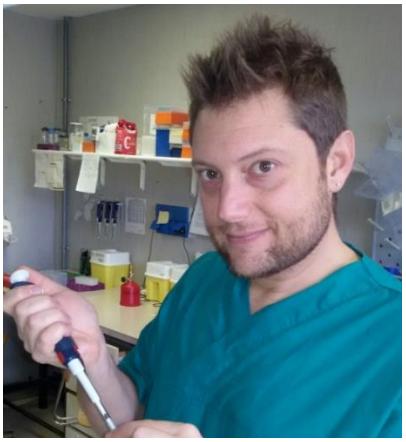


Figure 3. *Cell viability after 1 h exposure at several ed-OZO concentrations The graph shows the average and standard error of three different repetitions. * p<0.05; ** p<0.01; *** p<0.001.*

Recent Publications

1. Bellio, P., Mancini, A., Di Pietro, L., Cracchiolo, S., Franceschini, N., Reale, S., de Angelis, F., Perilli, M., Amicosante, G., Spyrakis, F., Tondi, D., Cendron, L., Celenza, G.Inhibition of the transcriptional repressor LexA: Withstanding drug resistance by inhibiting the bacterial mechanisms of adaptation to antimicrobials(2020) Life Sciences, 241
2. Bellio, P., Luzi, C., Mancini, A., Cracchiolo, S., Passacantando, M., Di Pietro, L., Perilli, M., Amicosante, G., Santucci, S., Celenza, G. Cerium oxide nanoparticles as potential antibiotic adjuvant. Effects of CeO 2 nanoparticles on bacterial outer membrane permeability(2018) Biochimica et Biophysica Acta - Biomembranes, 1860 (11), pp. 2428-2435
3. Bellio, P., Di Pietro, L., Mancini, A., Piovano, M., Nicoletti, M., Brisdelli, F., Tondi, D., Cendron, L., Franceschini, N., Amicosante, G., Perilli, M., Celenza, G. SOS response in bacteria: Inhibitory activity of lichen secondary metabolites against Escherichia coli RecA protein (2017) Phytomedicine, 29, pp. 11-18.
4. Bellio, P., Segatore, B., Mancini, A., Di Pietro, L., Bottoni, C., Sabatini, A.,Brisdelli, F., Piovano, M., Nicoletti, M., Amicosante, G., Perilli, M., Celenza, G. Interaction between lichen secondary metabolites and antibiotics against clinical isolates methicillin-resistant Staphylococcus aureus strains (2015) Phytomedicine, 22 (2), pp. 223-230.
5. Bellio, P., Brisdelli, F., Perilli, M., Sabatini, A., Bottoni, C.,Segatore, B., Setacci, D., Amicosante, G., Celenza, G. Curcumin inhibits the SOS response induced by levofloxacin in Escherichia coli (2014) Phytomedicine, 21 (4), pp. 430-434.



Biography

Pierangelo Bellio, PhD is a postdoctoral research fellow at the Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila (Italy). His research is devoted to the study of the mechanisms of resistance in pathogenic bacteria and fungi. He focuses his attention, from a microbiological and biochemical standpoint, on the use of natural or synthetic molecules as potential antimicrobials or antimicrobial adjuvants in order to resume old drugs and make them effective on multidrug resistance pathogens. Moreover, he is interested in exploiting bacterial SOS response as potential target to hinder the mechanism of acquisition of drug resistance in pathogenic bacteria.

Email: pierangelo.bellio@univaq.it

Notes/Comments: