Novel strategies to fight *Candida* infections: natural honey

M. E. Rodrigues, L. Fernandes, C. F. Rodrigues, A. Oliveira, M. Henriques

Centre of Biological Engineering (CEB), University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

University of Minho
School of Engineering

CENTRE OF BIOLOGICAL ENGINEERING

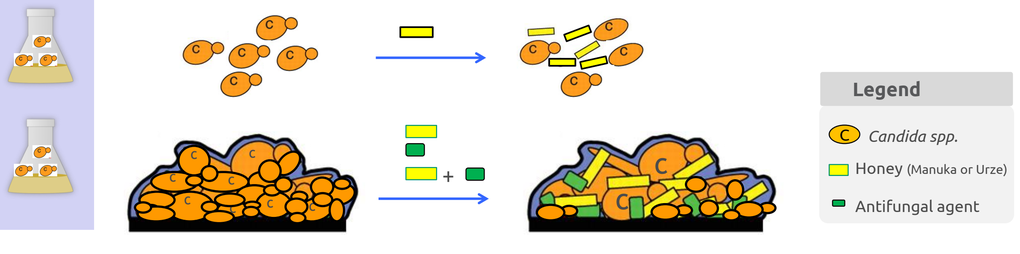
Introduction

The incidence of *Candida* infections (Candidosis) has increased remarkably in the last years, being attributed to the rise in the elderly population, the increasing number of immunocompromised patients, and the widespread use of indwelling medical devices. *Candida albicans* remains as the most prevalent species of these infections, but a clear rise in the proportion of non-*Candida albicans Candida* (NCAC) species has been noted. These species have an inherent level of resistance to certain antifungal agents higher than *C. albicans* though their virulence factors are much less understood. A major virulence factor is the ability to adhere and to form biofilms in medical devices and host tissues, because of a higher tolerance to antifungal therapy. Consequently, there is an urgent need to develop new strategies to fight these infections. Natural compounds are attracting increased interest in this field, among which honey. **AIM: To evaluate honey as a novel strategy to fight *C. tropicalis* infections.**

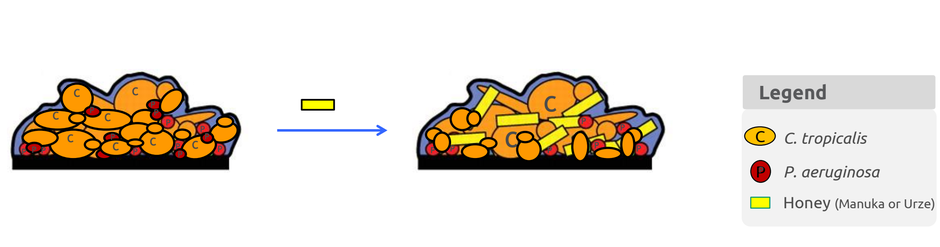
Methods

Honey (*Manuka* and *Urze)* was tested alone against *Candida (C. albicans; C. tropicalis; C. parapsilosis; C. glabrata)* planktonic cultures and in combination with antifungal agents (fluconazole, chlorhexidine, nystatin) against single and mixed (with *Pseudomonas aeruginosa*) biofilms.

Candida spp. planktonic and biofilms cultures



24 h biofilm of single and dual-species culture (*C. tropicalis* and *P. aeruginosa*)



- Effect of honey on planktonic cells (MIC)
- Effect of honey and honey + antifungal on single biofilms cells (CFUs and Live/Dead)
- Effect of honey on single and dual-species biofilms (CFUs)

Results

Effect of honey in planktonic *Candida* spp. culture

Table 1. MIC values of honey in *Candida* spp. planktonic cultures

	Urze	Manuka
C. albicans	50%	50%
C. tropicalis	25%	50%
C. parapsilosis	50%	50%
C. glabrata	50%	50%

Effect of honey in *C. tropicalis* biofilm culture

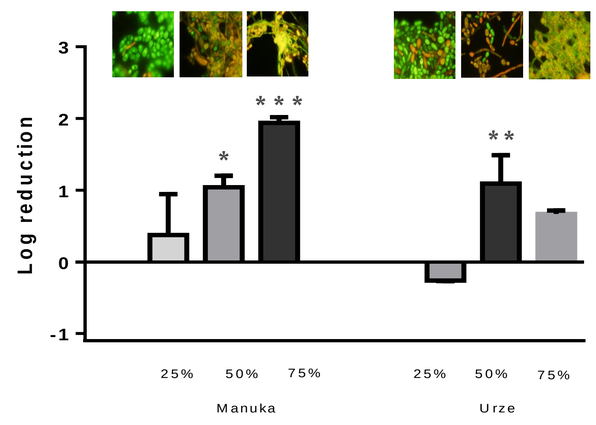


Figure 1. Therapeutic effect of honey against *C. tropicalis* biofilms.

Effect of honey + antifungal agents in *C. tropicalis* biofilms

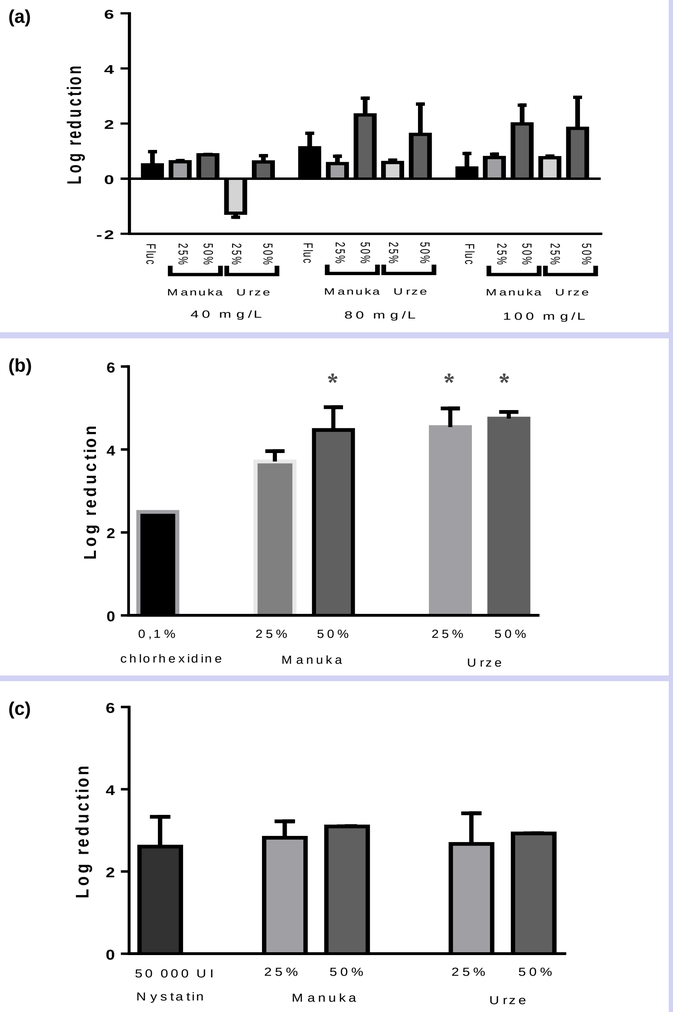


Figure 2. Therapeutic combined effect of honey and antifungal agents (Fluconazole (a); Chorhexidine (b); Nystantin(c)) against *C. tropicalis* biofilms.

Effect of honey activity in mixed- species biofilms

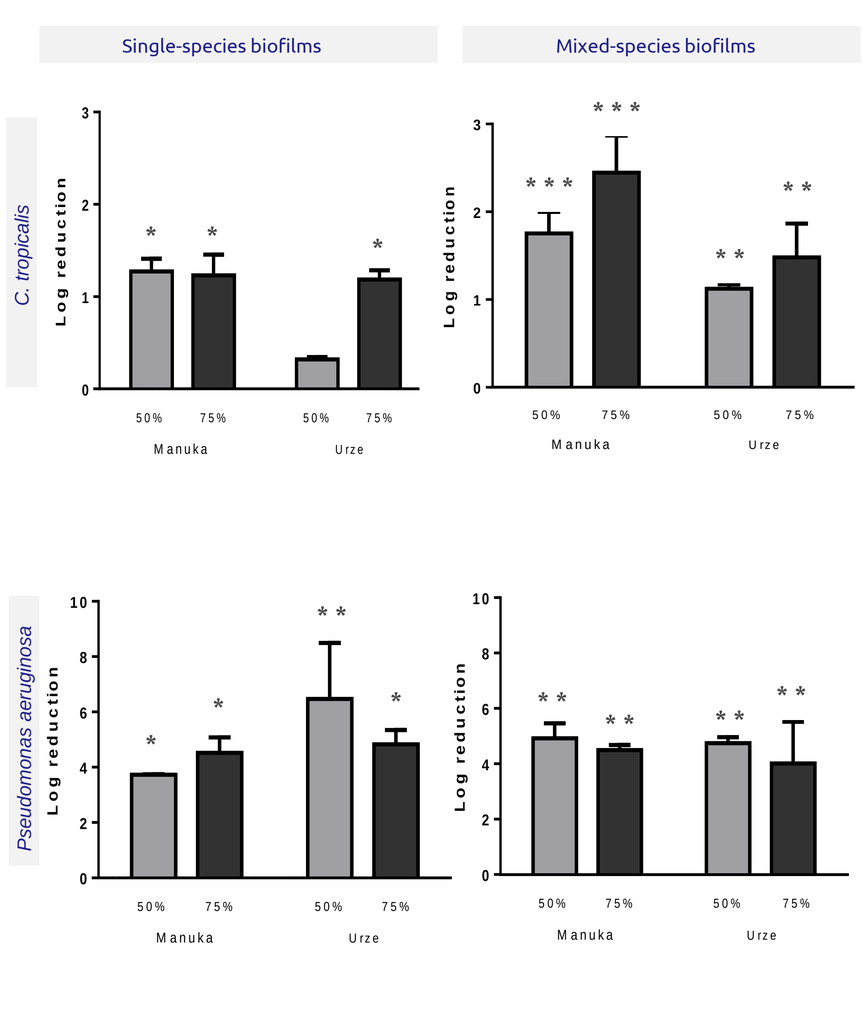


Figure 3. Therapeutic effect of honey against *C. tropicalis* and *Pseudomonas aeruginosa* mixed-biofilms cultures. (*P<0.05 compared with control)

Conclusions

- A first screening of the treatment with four planktonic *Candida* species culture indicated higher efficiency of honey against *C. tropicalis*.
- Honey is capable of 2-log reductions on *C. tropicalis* biofilms after 24h of treatment
- The combination of honey with nystatin and chlorhexidine reduces the antifungal dosage typically required in clinical settings by 50%, with a total biofilm reduction of 3-log with nystatin and 5-logs with chlorhexidine.
- In mixed biofilms of *C. tropicalis* and *P. aeruginosa,* honey at 50% or above reduces yeast and bacterial biofilm by 2-log and 4-log, respectively.

Altogether, our results highlight the great potential of honey as an alternative or complimentary strategy for the control of *Candida* infections.

This study was supported by FCT under the scope of the strategic funding of UID/BIO/04469/2013 unit and COMPETE 2020 (POCI-01-0145-FEDER-006684) and BioTecNorte operation (NORTE-01-0145-FEDER-000004) funded by the European Regional Development Fund under the scope of Norte2020 - Programa Operacional Regional do Norte.

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA
COMPETE 2020
PORTUGAL 2020
NORTE 2020
PROGRAMA OPERACIONAL REGIONAL DO NORTE
UNIÃO EUROPEIA
Fundo Europeu de Desenvolvimento Regional