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Research Article

RESEARCH ARTICLE

Effect of GAPDH-derived antimicrobial peptides on sensitive yeasts cells: membrane permeability, intracellular pH and H^+-influx/-efflux rates

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One sentence summary: *Saccharomyces cerevisiae* excretes AMPs derived from glyceraldehyde 3-phosphate dehydrogenase (GAPDH) that disturb the membrane integrity of sensitive yeast cells and compromise the pH homeostasis by increasing H^+-influx and decreasing H^+-efflux.

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ABSTRACT

Saccharomyces cerevisiae secretes antimicrobial peptides (AMPs) derived from glyceraldehyde-3-phosphate dehydrogenase (GAPDH), which induce the death of several non-*Saccharomyces* yeasts. Previously, we demonstrated that the naturally secreted GAPDH-derived AMPs (i.e. saccharomycin) caused a loss of culturability and decreased the intracellular pH (pHi) of *Hanseniaspora guilliermondii* cells. In this study, we show that chemically synthesised analogues of saccharomycin also induce a pHi drop and loss of culturability in *H. guilliermondii*, although to a lesser extent than saccharomycin. To assess the underlying causes of the pHi drop, we evaluated the membrane permeability to H^+ cations of *H. guilliermondii* cells, after being exposed to saccharomycin or its synthetic analogues. Results showed that the H^+-efflux decreased by 75.6% and the H^+-influx increased by 66.5% in cells exposed to saccharomycin at pH 3.5. Since H^+-efflux via H^+-ATPase is energy dependent, reduced glucose consumption would decrease ATP production and consequently H^+-ATPase activity. However, glucose uptake rates were not affected, suggesting that the AMPs rather than affecting glucose transporters may affect directly the plasma membrane H^+-ATPase or increase ATP leakage due to cell membrane disturbance. Thus, our study revealed that both saccharomycin and its synthetic analogues induced cell death of *H. guilliermondii* by increasing the proton influx and inhibiting the proton efflux.

Keywords: glyceraldehyde-3-phosphate dehydrogenase (GAPDH); mode of action; pH homeostasis, plasma membrane H^+-ATPase; glucose transporters; *Saccharomyces cerevisiae*

INTRODUCTION

Saccharomyces cerevisiae secretes antimicrobial peptides (AMPs) that induce death of several wine-related non-*Saccharomyces* yeasts, as a strategy to combat those microbial species during alcoholic fermentations (Albergaria *et al.* 2010; Branco *et al.* 2014; Albergaria and Arneborg 2016; Branco *et al.* 2017a). The natural biocide (i.e. saccharomycin) is composed by two main anionic

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