

Dissertation Abstract

The occurrence of *Candida auris* has been described as a global health threat since its first official identification in 2009. High mortality rates have been observed which are owed to its ability to establish invasive infections in a nosocomial manner as well as expressing multi-drug resistance. The development of novel antifungal drugs with unique targets is a growing necessity to combat this frequently occurring fungal pathogen and its virulence. Natural compounds and agents have been utilized for many generations to overcome infections. Now, scientific investigations of the mechanisms of action of certain phytochemicals have gained attention. The phenolic monoterpenes commonly extracted and isolated from essential oils are well recognized for their noteworthy anti-*Candida* activity, both *in vitro* and *in vivo*. This study focused on the antifungal activity as well as the oxidative stress capability of carvacrol, a monoterpene phenol, against *C. auris*.

The antifungal susceptibility profile of 25 clinical isolates of *C. auris* against carvacrol was determined by the use of the micro dilution broth method following CLSI guidelines. Carvacrol displayed growth inhibition in the range of 125 – 500 µg/ml and a fungicidal effect in the range of 250 – 1 000 µg/ml. *In vitro* analysis of oxidative stress caused by carvacrol was determined by the spectrophotometric observation of antioxidant enzyme levels as well as the gene regulation of these enzymes by reverse transcription quantitative polymerase chain reaction (RT-qPCR). The activities of the primary antioxidant enzymes (catalase, superoxide dismutase and glutathione peroxidase) showed an average fold increase in a range of 1.93 – 7.16 with an upregulation of gene expression in the range of 1.18 – 2.6 after carvacrol treatment at minimum inhibitory concentration (MIC). Conversely, secondary antioxidant enzymes (glutathione transferase and glutathione reductase) exhibited an average fold decrease of 4.88 and 2.18 as well as a downregulation of gene expression by 0.66 and 0.93 folds, after carvacrol treatment at MIC respectively. Lipid peroxidation, an indicator of oxidative stress, was also observed to be increased with an average of greater than 2-fold, after cells were treated with carvacrol at MIC values. Furthermore, cytotoxicity assays revealed that carvacrol at MIC values can cause 2.8 - 6.4 % haemolysis in the horse red blood cells, advocating its safe use during *in vivo* studies.

This study presented the potential of carvacrol to inhibit and eradicate *C. auris* by inducing increased levels of oxidative stress. Low MICs and killing property of carvacrol against *C. auris* isolates indicate that the carvacrol might be a potential candidate to develop into a novel antifungal agent.