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Treatment of the Candida subspecies *Candida albicans* and *Candida parapsilosis* with two far-UVC sources to minimise mycoses in clinical practice

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Abstract

Fungal infections have increased considerably over the last decades, becoming progressively resistant to common drugs. UVC light has shown microbiological eradication effects, whereby the wavelength of 254 nm is strongly carcino- and mutagenic. Therefore, 222 and 233 nm, which do not significantly harm skin cells, were tested for their antifungal effects. Microbicidal doses were reached at 40 mJ/cm^2 for both wavelengths, resulting in only minor superficial skin damage (<20 µm). UVC irradiation with far-UVC <240 nm represents a new opportunity to effectively eradicate even larger pathogens on tissue causing no or strongly reduced DNA and tissue damage.

KEYWORDS

233 nm UVC LED, Candida, clinical application, disinfection, fungal infections, mycoses

1 | INTRODUCTION

Fungal infections increased over the past decades, besides medicine's overall achievements and progress on various levels and across all dimensions. Fungal infections indeed show to have developed considerable resistance against respective treatments and drugs. It is therefore that this article describes a new way of fungal infection treatment.

Due to increasing drug resistance, fungal infections have considerably increased over the last decades.

In Europe, 7%–15% of all nosocomial infections are caused by fungal pathogens, predominantly by Candida subspecies. People with limited immune defence, including premature infants, elderly people, human immunodeficiency viruses and cancer patients, are mostly affected.[1] Currently, also COVID-19 patients show a higher probability for invasive mycoses.[2] A study representing 937 intensive care units showed that *C. albicans* and other non-*C. albicans* species are besides *S. maltophilia* and *Pseudomonas aeruginosa the pathogens reporting the highest mortality rate.*[3] Fungal infections causing a deadly course are always systemic. These systemic fungal

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infections mostly arise as an endogen infection from fungal colonisation or infection of the skin,[4] which makes it even more important to find new ways for effective treatment of fungal skin diseases.

UVC light has effective disinfection properties especially in reducing multi-resistant germs on surfaces in hospitals. Most conventional UVC disinfection devices are operated at wavelengths around 254 nm.[5] To minimise mutagenic effects, 222 nm UVC irradiation for microbiological eradication in vitro, ex vivo[6,7] and in vivo on murine skin[8] has been applied. UVC at a wavelength of 222 nm had a stronger germicidal effect on bacterial endospores than 254 nm, but its fungicidal effect is weaker than that of 254 nm UVC.[9] An irradiation at a wavelength around 233 nm using UVC LED represents an innovative possibility for the eradication of fungal pathogens. So far, it could be demonstrated that irradiation at 233 nm at a dose of 40 mJ/cm^2 can inactivate methicillin-resistant *Staphylococcus aureus* (MRSA) in different concentrations on blood agar plates.[10] Furthermore, 233 nm produces no or only little superficial DNA damage in excised human skin and reconstructed human epidermal (RHE) skin models up to 60 mJ/cm^2 in comparison to the same irradiation dose at 254 nm (≥factor 20); moreover, the DNA damage is below 0.1 of the minimal erythema dose UVB, which is considered acceptable. After 24 h, the DNA damage degraded completely in the RHE; multiple irradiation on four consecutive days with 60 mJ/cm^2 shows no detectable DNA damage.[11]

In this study, UVC irradiation at 233 nm was compared with 222 nm for its eradicating effect on the species *C. albicans* and *C. parapsilosis*; 254 nm served as a positive control for the possibility of complete eradication.

2 | MATERIAL AND METHODS

The eradicating effect on the fungal pathogens *C. albicans* and *C. parapsilosis* was examined with different UVC irradiation modules as previously described. UVC irradiation of the wavelengths 254 nm (0.24 mW/cm^2, LPL-R-01, Hg gas discharge lamp, sglux GmbH, Berlin, Germany), 233 nm (41 µW/cm^2, Ferdinand-Braun-Institut, Berlin, Germany)[10] and 222 nm (3.34 mW/cm^2, ExciJet222 30–130 Kit [111073] Kr-Cl Excimer lamp, USHIO Deutschland GmbH, Steinhöring, Germany) was applied. Doses of 10, 20, 40 and 80 mJ/cm^2 were investigated. Non-irradiated agar plates served as controls. The irradiance was controlled by the UV radiometer SXL55 with a SiC UVC sensor (sglux GmbH, Berlin, Germany).[10]

For the eradication experiments, the Candida species *C. albicans* and *C. parapsilosis* were prepared in four dilutions. In each case, 5 µl of the respective fungal cell suspension of low (1.0×10^1), intermediate (1.0×10^2), high (1.0×10^3) and very high (1.0×10^4) cell numbers was plated on Kimmig agar plates (PO5019A, OXOID, Wesel, Germany) containing 19 g/L glucose, 15 g/L peptone, 1 g/L NaCl, 5 g/L glycerine and 15 g/L agar. 30–60 min after application, the agar plates were irradiated. Afterwards, the plates were incubated at 37 °C, 5% CO_2 and 95% humidity for 48 h. To assess the eradication effect of the UVC LED 233 nm in comparison to 222 nm and 254 nm, the number of growing cultures was determined 2 days after irradiation. The eradicating effect of the different UVC LED wavelengths was evaluated by counting the colonies.

3 | RESULTS AND DISCUSSION

The non-irradiated controls of both Candida species grew well for all dilutions (Figure 1). From a highly concentrated Candida suspension (1.0×10^4), a confluent growth can be recorded.

An irradiation of the Candida species with 254 nm (positive control) at doses of 40 mJ/cm^2 leads to complete eradication of the cells for *C. parapsilosis*; for *C. albicans*, a complete eradication could be clearly shown for 480 mJ/cm^2. The application of 222 nm starts reduction at 10 mJ/cm^2 and shows a strong reduction in colony growth for both Candida species from an irradiation dose ≥20 mJ/cm^2. For 233 nm, the eradication process starts at a dose of 20 mJ/cm^2 for both Candida species. Compared to the non-irradiated control, the colony growth was reduced by at least 70% for *C. albicans* (Figure 2A) and *C. parapsilosis* (Figure 2B). At a dose of 40 mJ/cm^2, colony growth can be reduced by ≥98% (Figure 2), comparable with the wavelengths of 254 and 222 nm.

Our results are in agreement with the data from Narita et al.[9] where the fungicidal effect of 222 nm UVC against *C. albicans* is comparable with 254 nm UVC, a devastating effect could be demonstrated from 24 mJ/cm^2 compared to the control.

A dose of 40 mJ/cm^2 of 233 nm wavelength is capable of inactivating a broad spectrum of microbial pathogens, including fungal spores like Candida species (Figures 1 and 2). Compared to MRSA, fungal pathogens are at least a factor of 10–20 larger in size, making their eradication by far-UVC more difficult, but not impossible as shown in this research.

Fungal pathogens, which usually enter the human organism in the form of spores via the air or penetrate into the human organism via mucous membranes, become resistant to common active ingredients. Using LEDs emitting at 233 nm instead of excimer discharge lamps is a novel and innovative approach for preventing damage to genetic material and cells during disinfection of multi-resistant pathogens while at the same time benefitting from the smallness, compactness and robustness of these radiation sources.

The *in vitro* results will be used to derive irradiation protocols for far-UVC which can be used to eradicate microbes of various types and sizes on inanimate surfaces incompatible for chemical disinfection, in rooms (aerosols) and on the skin and mucous membranes without causing increased DNA damage. In addition, adapted far-UVC irradiation sources can also be used to reach regions of the body where local application of antiseptics is not fully possible. Furthermore, Candida species have the ability to form drug-resistant biofilms.[12] Further research is needed to assess the mode of action of far-UVC on biofilms.

In order to minimise the transmission of common fungal pathogens or other microbes between individuals (human to human or animal to human or vice versa), disinfection of rooms, grooming utensils or other items may be a good option.

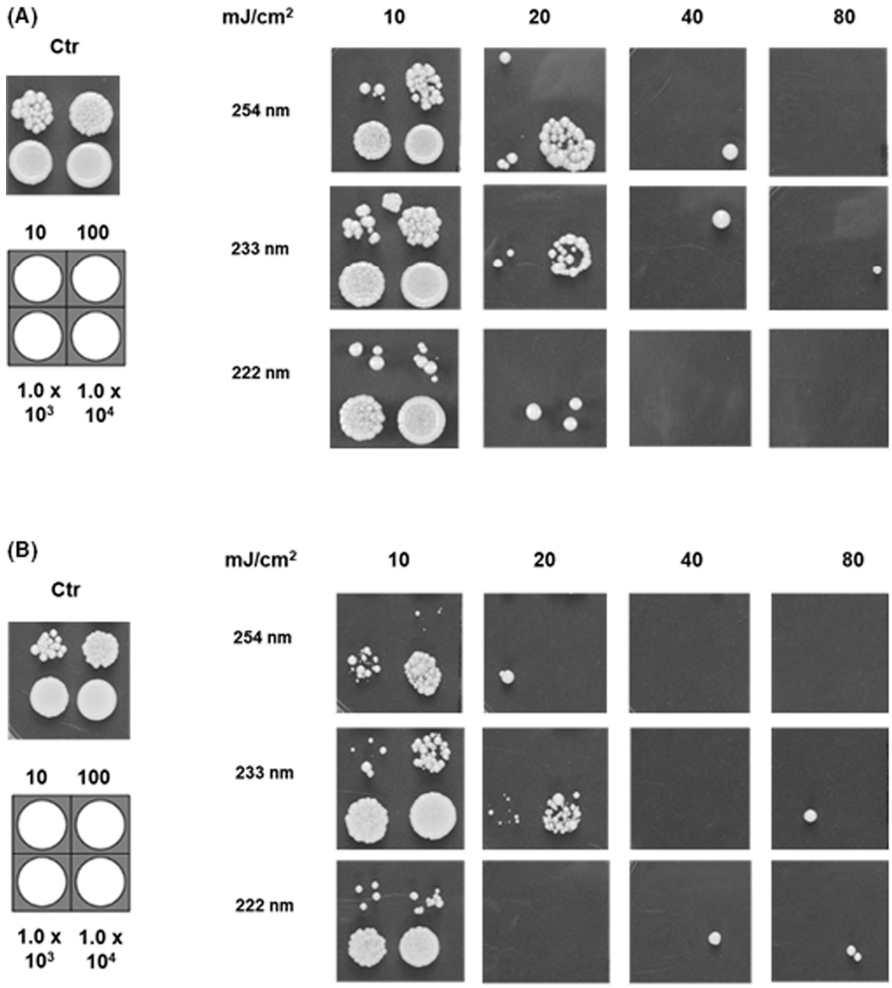

FIGURE 1 Colonisation of agar plates (exemplary presentation) with the Candida species *C. albicans* (A) and *C. parapsilosis* (B) after irradiation with the UVC irradiation modules of the wavelengths 222, 233 and 254 nm with the dose of 10, 20, 40 and 80 mJ/cm^2.

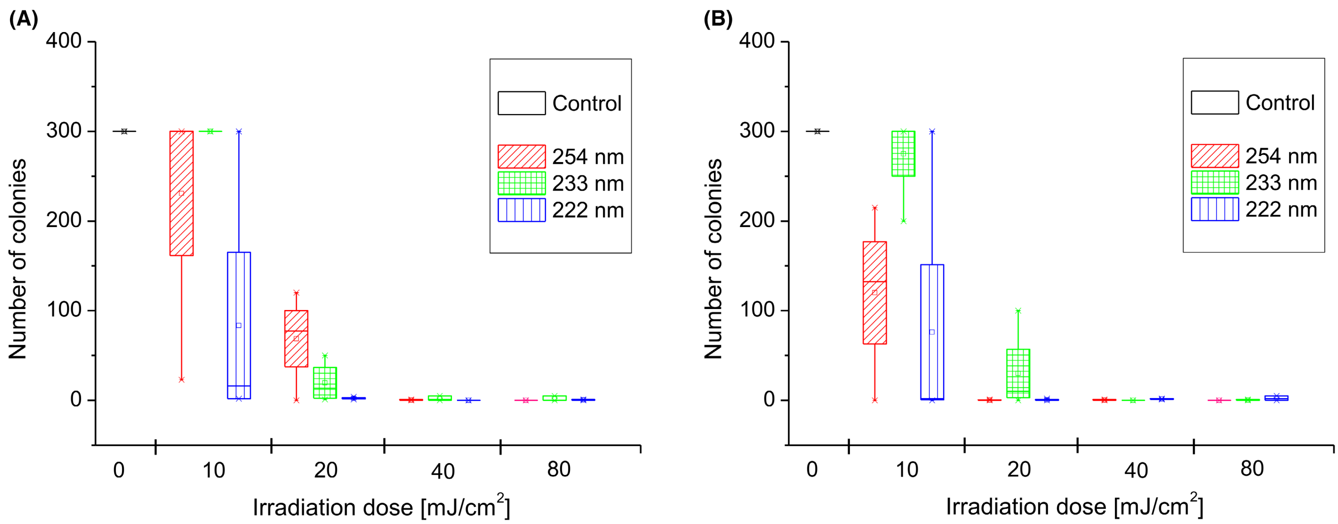

FIGURE 2 Number of colonies of the species Candida albicans (A) and Candida parapsilosis (B) from highly concentrated cell suspensions (1.0×10^4). Cultures were irradiated with either 10, 20, 40 or 80 mJ/cm^2 with the UVC wavelengths 222, 233 or 254 nm, ($n = 3$–4).

Another important application is the minimisation of athlete's foot. Filamentous fungi, so-called dermatophytes, are primarily responsible for athlete's foot infections (dermatophytosis). These fungi are widespread worldwide and can survive for many months outside the body.[13] Transmission of fungal spores occurs from person to person or through intermediary objects/contact surfaces, so further investigations in this direction are being sought.

Studies on human corneal and oral mucosal samples and *in vivo* studies are in progress.

4 | CONCLUSION

UVC irradiation at 233 nm and a dose of 40 mJ/cm^2 represents a new opportunity to effectively eradicate bacterial and yeast pathogens causing no or strongly reduced DNA and tissue damage on excised skin and RHE models. In terms of application, UVC irradiation at 233 nm might represent a good alternative to conventional disinfection methods.

AUTHOR CONTRIBUTIONS

J.S., S.B.L. K.G., J.E., M.C.M. conceived and designed the concept of the study and methodology, J.S., L.B., S.M., J.E. performed the experimental investigations, data analysis and interpretation of the data was done by J.S., S.B.L., N.L.P., S.V., J.E., M.C.M. Writing, review and editing, J.S., S.B.L., L.B., K.G., N.L.P., S.M., S.V., J.E., M.C.M. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data can be requested by interested working groups.

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