Skin and hard surface disinfection against *Candida auris* – What we know today

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Candida auris has emerged as a global healthcare threat, displaying resistance to important healthcare antifungal therapies. Infection prevention and control protocols have become paramount in reducing transmission of *C. auris* in healthcare, of which cleaning and disinfection plays an important role. *Candida albicans* is used as a surrogate yeast for yeasticidal claims of disinfection products, but reports have been made that sensitivity to disinfectants by *C. auris* differs from its surrogate. In this review, we aimed to compile the information reported for products used for skin and hard surface disinfection against *C. auris* in its planktonic or biofilm form. A comparison was made with other *Candida* species, and information were gathered from laboratory studies and observations made in healthcare settings.

KEYWORDS

skin disinfection, hard-surface disinfection, *Candida*, *Candida auris*, yeasticidal efficacy

1 Introduction

The first reported case of *Candida auris* was in 2009 when it was found in the external ear canal of an inpatient from Tokyo Metropolitan Geriatric Hospital ([1]). However, there is evidence that *C. auris* infections occurred as early as 1996 ([2]). Since then, it has been reported globally ([3–7]) and has become a major threat for healthcare settings according to the Centers for Disease Control and Prevention (CDC) ([8]), European Centre for Disease Prevention and Control (ECDC) ([9]) and the World Health Organization (WHO) ([10]). The WHO places *C. auris* together with *C. albicans* on the critical priority group for healthcare ([10]).

The undetected spread of *C. auris* is thought to be due to misidentification using conventional phenotypic methods, as it is fairly similar to other *Candida* species ([2], [11], [12]). However, major advances have been made in identifying *C. auris* using selective media and molecular diagnostic tools ([11], [13–17]). The greatest threat that *C. auris* poses is that it has shown to be resistant to important life-saving antifungal therapies in healthcare, such as fluconazole, amphotericin B, and echinocandins ([4], [18], [19]). So far, five clades of *C. auris* with a common ancestor have been identified containing antimicrobial resistance mutations and have been linked with invasive infections ([12]).

The genetic differences observed between the clades suggests that each clade emerged independently but simultaneously at different geographic locations ([4], [20]). Furthermore, each clade has been found far from its point of origin in different continents ([12], [20]). Clade I is generally associated with ear infections and is resistant to antifungal agents to a lesser degree ([12]). However, Clade II, III, IV and V have all shown resistance to fluconazole, cross resistance to amphotericin B and echinocandins, and some strains are pan-resistant ([12]).

Pan-resistance indicates that it is not susceptible to any clinically available antimicrobials. Therefore, the greatest threat that *C. auris* pose is its resistance to antifungal therapies important in healthcare.

The best solution to control *C. auris* transmission is using infection prevention and control methods, which include cleaning and disinfection of environmental surfaces and patient care equipment. In this review, the threat that *C. auris* pose to healthcare, its mechanism of persisting on skin and surfaces, and the current knowledge of cleaning and disinfection methods to control its transmission are discussed.

2 The threat that *C. auris* poses in healthcare facilities

When present on environmental surfaces, *C. auris* can survive in both dry and moist areas for long durations and has shown to survive up to 7 or 14 days (21, 22). When comparing survival, *C. auris* has a greater tendency to survive on surfaces than *C. albicans* but is similar to *C. parapsilosis* or *C. glabrata* (21). It appears that *Candida* species are often present on hospital environmental surfaces and have been found on floors, sinks and high touch areas, which could all be reservoirs for transmission (23). Since *C. auris* can be present on various objects for long durations, healthcare staff and patients can become contaminated after having contact with these surfaces (5). It is, therefore, essential to reduce the presence of *C. auris* in healthcare environments as the mortality rates of *C. auris* outbreaks in areas with critically ill hospitalized patients can range from 30 to 72% (24).

3 Mechanisms that contribute to the persistence of *C. auris* in healthcare settings

Candida auris differs from other *Candida* species genetically, but also shows differences in resilience and pathogenicity (4). Even though *C. auris* is considered less virulent than *C. albicans* (25), it has shown to undergo phenotypic transitions, and to form unique multicellular aggregates (26–32). It can also tolerate high salinity and temperatures up to 42°C (22, 33, 34). The ability of *C. auris* to form biofilms appear to be the main challenge that this yeast poses to healthcare as it can persist on human skin and environmental surfaces (21, 27, 35–37). It may resist removal efforts through standard cleaning and disinfection practices where the cleaning agent cannot disrupt or reach the biofilm.

The presence of *C. auris* on skin as biofilms is not unique and has been associated with other *Candida* species (38). A study conducted by Tharp et al. (39) suggested that *C. auris* is only present or occurs on an infected person's skin, but it was unclear whether *C. auris* was causing a dysbiosis of the skin microbiome or whether it was present as a result of the dysbiosis. The persistence of *C. auris* on the skin of patients is a great concern as living cells are continuously shed from the infected patient where it can contaminate sensitive environments in healthcare (40, 41). Horton et al. (36) compared the biofilm formation characteristics of *C. auris* with *C. albicans* in a laboratory study using skin niche conditions,

including porcine skin. The observations made in this study suggests that the advantage *C. auris* has compared to *C. albicans* is its ability to survive high saline conditions and environmental desiccation that might otherwise be challenging for *C. albicans*, thereby enabling its persistence in hospital environments.

The biofilm structure formed by *C. auris* seems to be similar to what is produced by other *Candida* species, which is rich in mannan-glucan polysaccharides (42, 43). The biofilm consists of multiple layers of accumulated yeast and the formed extracellular matrix traps fluconazole thereby reducing its concentration to a level where it is not efficacious anymore (42). However, this observation is not uncommon and drug tolerance has been already associated with the extracellular matrix of biofilms (44–46). The biofilm formed by *C. albicans*, *C. parapsilosis* and *C. glabrata* has all shown to negatively impact the outcome of patients (47–49).

Candida species, including *C. auris,* can be controlled with the correct cleaning and disinfection practices to minimize the spread of the environmental contaminants (23). Dry surface biofilms of *Staphylococcus aureu*s have shown to be resistant to important disinfectants in healthcare, i.e., sodium hypochlorite (50), and it might be similar for *C. auris*. For instance, recovery of *C. auris* aggregative cells were observed two weeks post-treatment with sodium hypochlorite (51). Using a three-dimensional biofilm model, Kean et al. (52) observed that matured *C. auris* biofilms can tolerate chlorhexidine and hydrogen peroxide treatment. The research covering the impact of disinfectants on *C. auris* planktonic cells and biofilms is limited, but what is known will be discussed in the subsequent sections.

4 The efficacy of skin disinfectants against *C. auris*

Infection prevention and control (IPC) protocols and screening methods are considered the best solution to reduce transmission (6), which will include skin cleaning and disinfection. For hand hygiene, the CDC recommends, among other practices, washing with soap and water and/or the use of alcohol-based hand sanitizers prior and after the use of gloves (53, 54). A similar recommendation is made by the Public Health England (PHE) and the Centre for Opportunistic, Tropical and Hospital Infections (COTHI). Currently, there are no recommended methods for decolonization or removing *C. auris* from the skin of an infected person (53). In the following sections the findings of skin cleaning and disinfection will be summarized and discussed.

4.1 Chlorhexidine as skin disinfectant

Chlorhexidine is a biocide often used in products targeted for skin disinfection and is known to be effective against *Candida* species (53, 55). It's a biocide known to target the microbial cell membrane (56). Using a suspension test (EN 13624:2013), Moore et al. (57) evaluated the efficacy of chlorhexidine against *C. auris.* The authors selected two products, one containing 2% w/v chlorhexidine with 70% (v/v) isopropyl alcohol (IPA), and the other contained 4% v/v chlorhexidine only. The products were diluted by 50% to simulate the addition of water, and the contact times ranged

from 30 s to 2 min (57). The outcome of the study showed that the diluted product containing chlorhexidine with IPA had a better performance after a 2 min contact time than the product containing chlorhexidine alone. The chlorhexidine together with IPA could reduce the counts of *C. auris* and *C. albicans* by ≥ 5-logs, but chlorhexidine alone could only reduce the counts of *C. auris* by ≤ 1-log even though the concentration was higher (57). Unlike *C. auris*, *C. albicans* was more sensitive to chlorhexidine alone and the log reduction ranged from 3.57-logs in clean condition to 3.36-logs in dirty conditions. The poor performance of chlorhexidine against *C. auris*, and the improvement observed when adding IPA, has been confirmed by another study conducted on porcine skin (58).

Rutala et al. (59) also confirmed the poor performance of chlorhexidine against *C. auris* and *C. albicans* when using 2% or 4% with a disk-based quantitative method and could confirm that *C. albicans* is more sensitive to chlorhexidine than *C. auris*. A product containing 1% chlorhexidine together with 61% ethyl alcohol was also tested (59), but it had a poor performance as only a 2-log reduction was observed for *C. auris* and a 1.9-log reduction for *C. albicans*. The contact time used was 1 min (59), which might be the cause for the lower performance. Taken together, these findings show that chlorhexidine is minimally efficacious against *C. auris* when used as the sole active ingredient, but when combined with alcohol the yeasticidal performance might substantially improve.

4.2 Alcohol-based skin disinfectants

To disinfect hands or skin to avoid the spread of *C. auris*, alcohol-based products are recommended. Alcohol is thought to target the microbial cell membrane, and essential protein, as its mode of action (56). Rutala et al. (59) made use of a disk-based quantitative carrier test with dirty conditions and used a contact time of 1 min to understand the performance of alcohol-based products against *C. auris*. The product containing 70% IPA was efficacious against both *C. auris* and *C. albicans* as a 3.8- and 4.1-log reduction was obtained, respectively. Similarly, 70% ethanol provided a 4-log reduction for *C. auris* but only a 2.5-log reduction was obtained for *C. albicans*. It seemed that ethanol was more efficacious against *C. auris* than *C. albicans* (59). Using a pig skin model, Fu et al. (60) assessed the efficacy of various alcohol-base products against *Candida* species, including *C. auris* and *C. albicans*. The authors observed that with a contact time of 1 min, alcohol-based products are sufficient to provide a 3-log reduction. This was observed when testing ethanol (54 to 66%) combined with n-propanol (9 to 11%), and when testing ethanol (75%) alone (60). The authors interestingly observed that when combining the alcohol with an additional product containing 0.1 to 0.2% p-chloroxylenol, the log reduction was similar but that the contact time was reduced to between 15 and 30 seconds (60).

4.3 Other products evaluated for skin disinfection

There are other products used for skin disinfection without chlorhexidine or alcohol. Povidone-iodine was tested at a 10% concentration (1% iodine) and was found to have a limited yeasticidal performance against *C. auris* as only a 2.5-log reduction was obtained (59). It also had a poor performance against *C. albicans* as only a 2.3-log reduction was observed. The contact time used was 1 min. These findings are in contrast with the observation made by Abdolrasouli et al. (61), which reported that 10% povidone-iodine provided sufficient efficacy against *C. auris* as an 8-fold reduction in growth was obtained when performing a suspension test in a 96-well microtiter plate. Moore et al. (57) used a standardized suspension test method (EN 13624:2013) and found that 10% povidone-iodine, when used at a 2 min contact time, could reduce *C. auris* and a clinically isolated *C. albicans* strain by ≥ 4-logs in both clean and dirty conditions. *C. albicans* strain ATCC 10231 typically used in EN methods, however, had only a 2.5-log reduction in clean condition and a 3-logs reduction in dirty conditions. *C. albicans* was thus less sensitive to 10% povidone-iodine (57). Iodine interacts with essential intracellular components such as proteins and nucleic acids, which leads to cell death (56)

An antiseptic containing 3% hydrogen peroxide showed to have a poor performance against *C. auris* as only a 1.4-log reduction was obtained (59). Similarly, only a 1.8-log reduction was obtained against *C. albicans*. Hydrogen peroxide is an oxidizing agent that produce free radicals which attach essential cell components for survival (56). Chloroxylenol was tested at a 1% concentration, and it was shown to have a better performance than 3% hydrogen peroxide. However, only a 2.8-log reduction was obtained against *C. auris* and a 3.9-log reduction when tested against *C. albicans* at a 1 min contact time (59). Chloroxylenol is a halophenol and its mode of action is thought to be the cell membrane (56). The results suggest that hydrogen peroxide or chloroxylenol might have a poor performance against *C. auris* when used as a skin disinfectant, but the information about the performance of these actives against *C. auris* are limited and might differ when the contact time is extended to more than 1 min.

5 Hard surface disinfectants tested against *C. auris*

For hard surface disinfection, the CDC suggests the use of Environmental Protection Agency (EPA)-registered products approved for healthcare and the ECDC recommends European Standards (EN)-registered products with antifungal claims (8, 9, 53, 62). The PHI suggests the use of 1,000 ppm hypochlorite (53). The COTHI suggests 1,000 ppm chlorine-releasing agents, and optionally hydrogen peroxide vapor (53). The WHO suggests cleaning with soap and water followed by disinfection with 0.1% bleach (1,000 ppm) (53). In the subsequent sections we compiled the most recent information available about the performance of hard surface disinfectants used in healthcare tested against *C. auris*.

5.1 Chlorine-based disinfectants

Chlorine-based disinfectants containing sodium hypochlorite or sodium dichloroisocyanurate are commonly used in healthcare settings to disinfect against methicillin-resistant *Staphylococcus aureus* (MRSA) or carbapenemase-producing bacteria (53).

Chlorine-based disinfectants typically causes oxidative damage to the cell membrane, and essential intracellular components (63). A study conducted during an outbreak at a United Kingdom hospital reported that chlorine-based disinfectants were sufficient at 1,000 ppm for daily routine disinfection of patient care areas and equipment to prevent *C. auris* (53, 64), and has been recommended by the WHO, PHI and COTHI. Moore et al. (57) utilized a standardized suspension test (EN 13624:2013) and showed that 1,000 ppm chlorine is efficacious against both *C. auris* and *C. albicans* as a ≥ 4-log reduction was obtained for both clean and dirty conditions when the contact time was 5 min. Rutala et al. (59) utilized a disk-based quantitative carrier test for two chlorine-based disinfectant products. The product contained 6,700 ppm sodium hypochlorite and was diluted to 670 ppm when tested against *C. auris*. This concentration showed to be sufficient to reduce *C. auris* by 4.1-logs and *C. albicans* by 4-logs, thereby confirming that a 1,000 ppm may be sufficient to target *C. auris*. The yeasticidal performance of chlorine-based disinfectants against *C. auris* has been confirmed in various studies, such as when using the quantitative carrier disk test method (ASTM E2197-11) (65), the EPA liquid disinfection test (EPA MLB SO MB-35-00) (66), a quantitative carrier disk test method (ASTM E-2197-02) (67) in a simulated room environment test (66) and using a microdilution method (61).

C. auris is expected to be present on environmental surfaces as biofilms. Therefore, it is essential to understand whether disinfectants can penetrate the protective layers of the biofilms and kill viable *C. auris* present. Limited information was available about the performance of chlorine-based products against *C. auris* biofilms, and the only study found was performed by Ledwoch et al. (68). The study combined a wipe test for bacteria (ASTM E2967-15) and a dry-biofilm method to assess the efficacy of chlorine-based disinfectants against *C. auris* dry biofilms when loaded onto wipes. Two products contained chlorine dioxide (300 ppm and 1,000 ppm), five contained sodium dichloroisocyanurate (1,000 ppm and 10,000 ppm), and two products contained sodium hypochlorite (500 and 1,000 ppm). These products had the same main active ingredient but differed in formulation composition. The authors investigated whether the wipe loaded with the product would reduce initial counts of the *C. auris* dry biofilm, whether the cells are transferable through the wipe, and whether regrowth will occur after cleaning (68).

The chlorine dioxide (1,000 ppm) product performed poorly as only a 2.5-log reduction was observed, the product transferred *C. auris* after cleaning, and regrowth post-wiping was observed after 2 days (68). Only one out of the five sodium dichloroisocyanurate products reduced the *C. auris* biofilm by ≥ 4-log, showed low transferability. Regrowth of *C. auris* was observed after 4 days. This product contained the co-formulants adipic acid, sodium toluene sulfonate, and sodium-N-lauroyl sarcosinate, in addition to the 1,000 ppm sodium dichloroisocyanurate. The product containing 1,000 ppm sodium hypochlorite reduced the *C. auris* by ≥ 7-logs and none of the *C. auris* cells picked up by the wipe was transferred to a new surface. However, regrowth was observed within 2 days. It appears that chlorine-based products containing sodium dichloroisocyanurate or sodium hypochlorite at 1,000 ppm are the best performing biocidal actives against *C. auris*, but its performance is dependent on the composition of the final formulation (68).

5.2 Quat and Quat-alcohol-based disinfectants

Quat is favored in many healthcare facilities due to the fungicidal, bactericidal and virucidal activity of various quat-based disinfectants (53). However, laboratory studies show that quat-based disinfectants have a poor performance against *C. auris,* and it has been implied to be the cause for an outbreak in an intensive care unit (ICU) at the Oxford University Hospital in 2018 (69). Quats are cationic surfactants that destabilizes the cell membrane, and targe essential enzymes, leading to cell lysis and eventual cell death (56, 63). The performance of quat-based products was tested against *C. auris* using a disk-based quantitative carrier test with a contact time of 1 min (59). One product contained a combination of octyl decyl dimethyl ammonium chloride (ODDMAC; 6.51%); dioctyl dimethyl ammonium chloride (DODMAC; 2.604%); didecyl dimethyl ammonium chloride (DDDMAC; 3.906%) and alkyl dimethyl benzyl ammonium chloride (ADMBAC; 8.68%). The product was diluted to have a concentration of 0.08% total quat in use. The authors observed only a 1.7-log reduction for *C. auris* and 1.5-log for *C. albicans*. A quat-based product combined with an alcohol, containing 0.1% quat with 58% ethanol in use, reduced the *C. auris* counts by 3.8-log, and the *C. albicans* counts by 4.1-log (59). These findings suggested that quat on its own has a relatively poor performance against key yeasts, and that the addition of alcohol to quat improves its performance. Other studies support the poor performance of quat against *C. auris* when used at about 0.1% quat, using a quantitative carrier test (EPA MLB SOP MB-35-00) (70, 71), and ASTM E2197-11 (65), and when used in a disinfectant wipe test (72). Even quat-based products that had supported fungicidal claims against *C. albicans* failed against *C. auris* (71), which highlights that even though a formulation has fungicidal or yeasticidal claims against *C. albicans*, it might not be similarly efficacious against *C. auris*. When the products were tested at a 10 min contact time, the log reduction was still insufficient (65, 71).

The co-active used together with quat does not necessarily need to be an alcohol. For instance, Müller et al. (73) used a suspension test (EN 13624) and a surface test with mechanical action (EN 16615) to evaluate the efficacy against *C. auris* and *C. albicans* of a quat-based product that was combine with co-actives. The product tested contained 22% ADBAC/BKC, 17% 2-phenoxyethanol, 0.9% amines N-C12-C14 (even numbered)- alkyltrimethylenedi-, reaction products with chloroacetic acid. When diluted to 0.25%, the product contained 0.06% ADBAC/BKC, 0.04% phenoxylethanol and 0.003% amine. The diluted product could reduce both yeasts by ≥ 4-logs when the suspension test was used with a 2 min contact time, and when using the surface test with a 1 min contact time (73).

When testing a quat-based product against *C. auris* dry biofilm, Ledwoch et al. (68) observed that the product was able to reduce the initial *C. auris* counts of the dry biofilm by 4-logs. The sufficient yeasticidal performance observed against *C. auris* could be due to mechanical removal when using the wipe or it could be due to the higher concentration of quat used in the product. The product contained benzalkonium chloride (BAC) and polyhexamethylene biguanide (PHMB) at a total concentration of 5,000 ppm (0.5%) quat. A low concentration of DDAC was also present. In this study,

the quat-based product also prevented the transferal of about 80% of the picked-up yeast to another surface and was able to prevent regrowth for 2 days after treatment.

5.3 Hydrogen peroxide and peracetic acid as disinfectants

Non-quat-based disinfectants used in healthcare could contain hydrogen peroxide (HP) or peracetic acid with acetic acid (PAA). Both actives are oxidizing agents that denatures proteins and increase the permeability of the cell wall (56). Cadnum et al. (65) used the quantitative carrier disk test method (ASTM E2197-11) to evaluate the performance of peroxides against *Candida* species. A product containing 1.4% hydrogen peroxide was tested at a 1 min contact time and another containing 0.5% hydrogen peroxide was tested at a 10 min contact time. A disinfectant containing 12,000 ppm peracetic acid was also tested at a 3 min contact time. All these products reduced *C. albicans*, *C. glabrata* and *C. auris* by ≥ 5-logs. A similar observation was made by Rutala et al. (59) when using a disk-based quantitative carrier test, by Haq et al. (70) and Sexton et al. (71) using the quantitative carrier test (EPA MLB SOP MB-35-00), by Voorn et al. (72) using a wipe test, and by Cadnum et al. (67) when using a quantitative carrier test. However, yeasticidal performance is formulation dependent. For example, when testing an antiseptic that contains 3% hydrogen peroxide in use, the product had a poor performance against both *C. auris* and *C. albicans* as less than 2-log reduction was obtained (59). However, a disinfectant containing 1.4% hydrogen peroxide reduced both yeasts by 4-logs. Both products were tested with a 1 min contact time (59).

Kean et al. (74) tested the performance of 2,000 ppm peracetic acid on various carrier materials and obtained a 4-logs reduction of *C. auris*, *C. glabrata* and *C. albicans* after a contact time of 5 min. Notably, one out of the four *C. auris* strains tested was less sensitive to peracetic acid and was only reduced by about 3-logs. The carrier materials used were polyester polymer, stainless steel and cellulose matrix. However, even though the yeast counts could be reduced sufficiently, regrowth was observed after treating the adhered *C. auris* on stainless steel or polyester. Regrowth was not observed on the porous cellulose matrix (74).

Regrowth of *C. auris* after treatment with peracetic acid-based products was also assessed against dry-biofilms by Ledwoch et al. (68). Two products were tested containing 3,500 ppm peracetic acid, which is higher than the previously mentioned study. The authors reported a ≥ 7-logs reduction of the initial *C. auris* counts when treating a dry biofilm. Regrowth of *C. auris* after cleaning was only observed after 6 days. No yeast was transferred from the wipe after cleaning, which indicates the active could kill the yeast cells removed from the surface (68). These findings suggest that peracetic acid used at the reported concentration is efficacious against *C. auris*, it could eliminate dry biofilms and prevent regrowth shortly after cleaning.

Hydrogen peroxide was also evaluated as a vapor and was used at 8 g peroxide per cubic meter room (61). The authors tested the vapor on desiccated *C. auris* cells in a 96-well microtiter plate

and obtained no viable cells after the treatment time. Hydrogen peroxide vapor was also combined with a chlorine-based cleaner (1,000 ppm) as part of a regular disinfection regime, and it was observed to aid the controlling of *C. auris* during an outbreak in a UK-based hospital (64). These findings suggest that HP or PAA-based products might be an alternative to quat-based disinfectants.

5.4 Other products tested as hard surface disinfectants

There are other biocidal products commercially available as hard surfaces disinfectants, but information about their performance against *C. auris* is limited. An alcohol-based product containing ethanol at 12% with 17.5% propan-1-ol was tested using a suspension test (EN 13624) and a surface test with mechanical action (EN 16615) (73). *C. auris* counts could be reduced by ≥ 4-logs using both test methods (73). Glutaraldehyde was tested at 2.4% using a quantitative carrier test method (59). A contact time of 1 min was used and the product could reduce both *C. auris* and *C. albicans* by 4.1-logs. Glutaraldehyde targets the microbial cell envelope and cross-links essential macromolecules (56). Ortho-phthalaldehyde was used at 0.55% and gave a 2.3-log reduction when tested against *C. auris* and 3.8-log reduction against *C. albicans*. A diluted product containing 0.07% *o*-phenylphenol with 0.06% *p*-tertiary amylphenol reduced *C. auris* by 4.1-logs and *C. albicans* by 3.6-logs when a 1 min contact time was used (59). The results obtained after treatment with the latter two products highlighted that there could be a difference in susceptibility between the two *Candida* species.

5.5 Ultraviolet light (UV-C) as a non-chemical hard surface disinfection method

No-touch disinfection methods, such as UV-C, are considered beneficial for treating hospital surfaces after manual cleaning and/or disinfection has been employed as some areas might have been missed or cleaned improperly. UV-C is known to cause damage to nucleic acids in the microbial cell (75, 76). Cadnum et al. (77) tested the impact of UV-C of healthcare relevant *Candida* species in comparison with MRSA and *Clostridium difficile*. The authors found that at 1.5 meters, MRSA was more susceptible to UV-C than *C. auris*, *C. albicans* and *C. glabrata* and *C. difficile* when exposed for 10 min. *C. auris* was the least sensitive *Candida* specie tested. *C. auris* had less than a 2-log reduction, and *C. albicans* and *C. glabrata* had less than a 3-log reduction after a 10 min exposure. However, after 20 min a more than 4-log reduction was observed for all the *Candida* species tested. When an exposure time of 30 min was used, the reduction went higher than 5-logs (77). This suggests that UV-C treatment is effective against Candida, but the exposure time is longer than what is typically used for bacteria. In contrast with the observations made by Cadnum et al. (77), Fu et al. (60) could obtain ≥ 3-logs reduction for various *Candida* species, including *C. auris* and *C. albicans*, when exposed at 1 meter for 10 min and 2.5 meter for 1 hr, which further improved when

treated for a longer period (60). The *C. auris* isolates used in the study performed by Fu et al. (60) were clinical isolates from patients located in India, and Cadnum et al. (77) used clinical isolates from Germany and an isolate that showed antifungal sensitivity. The difference in observations when testing UV-C by the two separate studies could be due to the fact that different clades were being used as *C. auris* test subjects and/or the differences in UV-C doses delivered. Previous studies have reported differences in sensitivity to disinfection strategies between strains in the same clade, and between different clades (78–80), and an association between a reduced sensitivity and the aggregating phenotype has been drawn (78, 80). Overall, various studies confirmed the efficacy of UV-C against *C. auris*, but its performance depends on the dose delivered (i.e., treatment distance and exposure time) (11, 53, 81–83). The data obtained by Chatterjee et al. (78), was the only study reporting a poor performance against *C. auris* as less than 1-log reduction was obtained after a 30 min exposure time for all the clades tested.

6 Conclusion

Standardized biocidal efficacy methods were established to ensure that claims made by manufacturers regarding the product's antimicrobial efficacy are reliable, reproducible and scientifically valid. These laboratory methods aim to represent "real-world" scenarios but are actually controlled conditions. "Real-world" scenarios are often complex that cannot be fully captured by standardized methods or other laboratory tests, such as whether the manufacturer's guidelines were being followed. Therefore, these tests should be interpreted in the context of their limitations. In this review, we observed various studies showing the antimicrobial efficacy of disinfectant products against *C. auris*, amongst other *Candida* species, in laboratory settings. Limited information about the performance of these products is known in the "real-world."

Laboratory studies suggest that quat-based products used for hard surface disinfection have limited performance against *Candida*. However, combining quat with an additional biocidal compound appears to be sufficient to improve its performance. A similar observation was made for chlorhexidine typically used for skin disinfection. Therefore, the use of quat-based products or chlorhexidine-based products should be used with the awareness that its performance depends on the formulation composition, the biocide concentration and contact time used. This point could be made of all disinfection products, irrespective of the main biocidal active present.

From studies performed on both skin and hard-surface disinfectants, it was clear that there are differences in sensitivity between *C. auris* and *C. albicans*. This difference in sensitivity was not atypical compared to other *Candida* species, such as *C. glabrata* or *C. parapsilosis*. Disinfectants with fungicidal or yeasticidal claims against *C. albicans* also showed to not be equally efficacious against *C. auris*, and differences in sensitivity between *C. auris* clades or strains were observed. These findings suggest that biocidal products should be approved for *C. auris* claims in addition to *C. albicans* when used in a healthcare setting. When testing the efficacy of a disinfectant product against *C. auris*, the clade or strain selection as a test subject should also be considered.

The unique aggregating phenotype of *C. auris* was associated with a lower sensitivity to disinfectants compared to other *Candida* species, but further research is required to understand the role that aggregation plays in the persistence or reduced sensitivity of *C. auris*. Various studies discuss the importance of biofilm formation in the persistence and transmission of *Candida*, including *C. auris*, in healthcare but only one study performed by Ledwoch et al. (68) tested various disinfectants against *C. auris* dry biofilms. Variations in efficacy between formulations with the same concentration of biocidal active ingredient was observed, but most importantly some products were unable to prevent transferring the yeast from the wipe after cleaning. Regrowth of *C. auris* after a few days of cleaning was observed and it differed between the products tested. The latter two observations are important as it might be contributing to the persistence and transmission of *C. auris* in healthcare.

In conclusion, resistance to antifungal drugs does not mean *C. auris* cannot be controlled by using cleaning and disinfection products. The findings reviewed here confirmed that efficacy still remained dependent on the composition of the formulations and not on the single biocide active present in the product. A difference in sensitivity was observed between *C. auris* and *C. albicans*, and it might benefit healthcare facilities to have a combination of both *C. auris* and *C. albicans* claims for relevant disinfection products.

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Publisher's note

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