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Clade-dependent resilience of *Candidozyma auris* challenges surrogate-based disinfectant testing: implications for efficacy testing of oxidative disinfectants

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SUMMARY

Background: *Candidozyma auris* has emerged as a globally relevant healthcare-associated pathogen characterized by environmental persistence, outbreak potential, and multi-drug resistance. Current yeasticidal disinfectant efficacy testing relies on *Candida albicans* as the standard surrogate organism. However, emerging evidence suggests that susceptibility may vary by clade, active substance, and formulation, questioning the universal adequacy of surrogate-based testing.

Aim: The aim of this study was to determine whether *C. albicans* adequately serves as a surrogate organism for yeasticidal disinfectant efficacy testing against *C. auris*, with particular focus on oxidative disinfectants, especially peracetic acid–based formulations.

Methods: A stepwise comparative design was applied. Standardized quantitative suspension testing assessed intrinsic susceptibility differences between *C. albicans* and

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Disinfectant efficacy testing

C. auris using defined active substances. Subsequently, commercially available oxidative disinfectant products were evaluated under standardized application-relevant conditions. *C. auris* isolates representing different phylogenetic clades were included to assess clade-dependent susceptibility differences.

Findings: *C. auris* showed susceptibility comparable to or greater than that of *C. albicans* for alcohols, aldehydes, and quaternary ammonium compounds. In contrast, marked differences emerged for peracetic acid—based disinfectants. Several oxidative products demonstrated robust yeasticidal efficacy against all tested organisms, whereas selected peracetic acid—based products showed reduced efficacy against *C. auris*. The most pronounced differences were observed for clade I isolates.

Conclusion: Surrogate-based yeasticidal efficacy testing using *C. albicans* remains appropriate for most disinfectant product groups. However, for selected peracetic acid—based formulations, this approach may not universally provide a reliable assessment. Targeted inclusion of *C. auris* may therefore refine efficacy testing in selected scenarios.

Introduction

Candidozyma auris (formerly *Candida auris*) has emerged as a major healthcare-associated pathogen characterized by rapid global spread, multi-drug resistance, and a pronounced ability to persist in the healthcare environment [1,2]. Since its first description, *C. auris* has been reported in more than 60 countries, with outbreaks increasingly transitioning from sporadic introductions to endemic transmission in several regions [1—3]. Surveillance data from the USA and Europe demonstrate a continuous increase in reported case numbers, underlining the growing relevance of this pathogen for infection prevention and control, although the overall burden remains relatively low in many regions [4,5].

In addition to patient colonization, environmental contamination plays a key role in the transmission of *C. auris*. The organism is able to persist on surfaces and medical devices and can withstand routine cleaning and disinfection procedures, thereby contributing to nosocomial spread [6,7]. These characteristics highlight the importance of effective disinfectant strategies in controlling *C. auris* transmission.

Recent evidence challenges the previously suggested concept of generalized reduced susceptibility or cross-resistance of *C. auris* to disinfectants. While earlier interpretations implied an overall increased tolerance, current data, including studies on clinical isolates and adaptive susceptibility changes following biocidal exposure, indicate that disinfectant efficacy is highly dependent on the active substance, formulation, and test conditions rather than representing a uniform resistance phenotype [8—11]. The recently introduced concept of replication capacity after use (RCAU) further emphasizes that disinfectant susceptibility must be interpreted in relation to defined use conditions and clinically relevant endpoints [8].

A further layer of complexity arises from the genetic diversity of *C. auris*, which comprises several phylogenetic clades that differ not only in geographical distribution but also in phenotypic characteristics, including susceptibility to disinfectants [12,13]. Recent work has demonstrated that clade I, which is increasingly reported in Europe and the USA, may exhibit increased RCAU compared with other clades and *Candida albicans*, the standard surrogate organism used in yeasticidal disinfectant efficacy testing [3,4,12,13]. Consequently, *C. auris* does not exhibit uniform behaviour across disinfectant classes, with certain product groups remaining highly effective while others show reduced or more variable performance [13,14]. This conceptual shift has important implications for disinfectant testing, as surrogate-based assumptions may not reliably capture the full spectrum of clinically relevant susceptibility patterns in all contexts, raising the possibility that additional evaluation with *C. auris* may be justified in selected scenarios [13,14].

Despite the increasing relevance of *C. auris*, most disinfectant efficacy testing frameworks continue to rely on *C. albicans* as a surrogate organism for yeasticidal activity [14—17]. Although this approach is well established, it remains unclear whether *C. albicans* adequately reflects the susceptibility of *C. auris*, particularly in light of clade-dependent variability and the concept of RCAU.

The aim of this study was therefore to assess whether *C. albicans* can be considered an adequate surrogate organism for yeasticidal disinfectant efficacy testing against *C. auris*. Additionally, we aimed to evaluate clade-dependent differences in susceptibility and investigate whether currently marketed disinfectant products maintain reliable yeasticidal efficacy against *C. auris*, with particular focus on oxidative disinfectants, especially peracetic acid (PAA)—based formulations.

Methods

Study design

A stepwise experimental approach was applied to investigate both intrinsic antimicrobial susceptibility and formulation-dependent efficacy. In an initial phase, defined active substances were evaluated using quantitative suspension tests. In a second phase, commercially available disinfectant products were tested to assess their efficacy under standardized conditions.

To enable methodological comparison, quantitative suspension tests according to VAH methods 9 and 20 were performed in parallel during the initial screening phase. This allowed direct assessment of potential differences between both test approaches [18,19].

Test organisms

The study included *C. auris* isolates representing clade I (DSM 105992, South Asian lineage), clade II (DSM 21092, East Asian lineage), clade III (DSM 105998, African lineage), and clade IV (DSM 105991, Venezuelan lineage), as well as the reference strain *C. albicans* DSM 1386, which served as the surrogate organism in accordance with established disinfectant testing standards for yeasticidal activity [15,16]. Clade assignment of *C. auris* isolates was based on prior molecular characterization.

Culture conditions and inoculum preparation

All organisms were cultured and prepared in accordance with established European disinfectant testing standards and VAH methodologies [15,16]. Yeast strains were maintained on appropriate agar media and subcultured at least once before testing to ensure metabolic activity and reproducibility.

For each experiment, fresh cultures were used to prepare standardized test suspensions. Cells were harvested, resuspended in an appropriate diluent, and adjusted to the required test suspension of 1.5 to 5.0 $\times$ 10^7 cfu/mL. Homogeneous suspensions were ensured to minimize variability due to aggregation.

Following exposure to disinfectants, samples were immediately neutralized using validated neutralizing agents to prevent residual antimicrobial activity. Neutralization efficacy was verified in accordance with the requirements defined in VAH methods and corresponding European standards [15–17]. Neutralized suspensions were serially diluted and plated on appropriate agar media. Colony-forming units were determined after incubation under defined conditions.

Comparative susceptibility testing of C. albicans and C. auris to selected active substances

Initial screening experiments were conducted using representative active substances or reference formulations to compare intrinsic susceptibility patterns independent of commercially marketed end-use products. The tested substances included isopropanol (IPA), glutaraldehyde (GA), PAA (represented by Lerasept Special), and didecyldimethylammonium chloride (DDAC; represented by Barquat). Quantitative suspension tests were performed in parallel according to VAH methods 9 and 20 [18,19]. Following exposure, suspensions were neutralized, serially diluted, and plated on malt extract agar (MEA) for quantitative recovery.

Testing was carried out using *C. albicans* and a representative *C. auris* clade II strain, which served as the established laboratory strain commonly used in initial experimental studies.

Comparative susceptibility testing of C. albicans and C. auris to selected marketed products

Commercially available disinfectant products (products A–G; Table I) were evaluated using quantitative suspension tests according to VAH method 20 [19]. Product selection focused on oxidative formulations based on PAA and chlorine dioxide.

Testing included *C. albicans* and *C. auris* isolates representing clades I, III, and IV to assess clade-dependent differences in susceptibility under application-relevant conditions. All products were tested at their respective use concentrations and defined contact times according to their current VAH listing conditions [20]. Where appropriate, additional conditions spanning the transition from insufficient to effective – called the intermediate – yeasticidal activity were included to enable discrimination of relevant susceptibility differences between test organisms. Following exposure, suspensions were neutralized in TLH sodium thiosulfate neutralizer (Tween/polysorbate 80, lecithin, L-histidine, and sodium thiosulfate), serially diluted, and plated on MEA for quantitative recovery.

Test procedure and evaluation criteria

Commercial disinfectant product testing was performed using quantitative suspension tests according to VAH method 20 [19], representing the German VAH equivalent of the European quantitative suspension test framework for yeasticidal efficacy testing as defined in EN 13624 [16] within the overarching framework of EN 14885 [17]. Initial active substance screening was primarily conducted to assess intrinsic susceptibility

Table I
Overview of the disinfectant products included in the study, including active substance declarations, organic load, and concentration–time ratio as certified for yeasticidal efficacy and listed by the VAH

Product	Active substance(s)	Organic load	Concentration–time ratio
Product A	Peracetic acid (10.7–13.5 g/100 mL)	Dirty condition	30 min – 0.75% + 0.75%[a]
Product B	Peracetic acid (0.06%/100 g (w/w))	Dirty condition	1 min – concentrated
Product C	Peracetic acid (5 g/100 g)	Clean condition	5 min – 1%
		Dirty condition	5 min – 2%/60 min – 1%
Product D	Peracetic acid 1% (>750 ppm)	Clean condition	5 min – 1%/15 min – 0.5%
		Dirty condition	30 min – 1%/60 min – 0.5%
Product E	Hydrogen peroxide (7 g/100 g), glycolic acid (0.1 g/100 g), and peracetic acid (1000 ppm/100 g)	Dirty condition	5 min – concentrated
Product F	Chlorine dioxide in aqueous solution (0.15 g/kg [150 ppm])	Clean condition	5 min – concentrated
Product G	Chlorine dioxide in aqueous solution (0.0175–0.0225%, w/v)	Clean condition	1 min – concentrated

Clean condition/low organic load: 0.3 g/L bovine albumin; dirty condition/high organic load: 3 g/L bovine albumin + 3 g/L erythrocytes.
[a] Components A and B mixed in a 1:1 ratio.

differences independent of formulation effects. Within the initial screening, testing according to the established VAH method 9 [18] was included to allow methodological comparison with the newly introduced microscale VAH method 20 [19].

Test suspensions were exposed to disinfectants under defined conditions, followed by immediate neutralization after the specified contact times. Only test runs fulfilling all validity criteria, including appropriate control performance and verified neutralization efficacy, were included in the analysis.

Efficacy was determined by calculating the logarithmic reduction in viable counts relative to control samples and interpreted according to the acceptance criteria for yeasticidal activity defined in the applicable VAH methods [18,19].

Testing was performed in accordance with applicable VAH and EN methodological requirements, including at least the required independent experimental runs with evaluation of three defined concentrations and three exposure times, depending on the respective test system.

Results

Comparative susceptibility of C. albicans *and* C. auris *to selected active substances*

Representative comparative testing under selected VAH method 9 conditions demonstrated substance-dependent differences between *C. albicans* and *C. auris* clade II (Figure 1). A comprehensive overview of all tested conditions, including comparison with VAH method 20, is provided in Supplementary Figure SI. For alcohol-based (IPA) and aldehyde-based (GA) conditions, *C. auris* generally showed comparable or greater susceptibility than *C. albicans*. Similar observations were obtained for DDAC, where no relevant reduction in susceptibility of *C. auris* compared to *C. albicans* was observed.

In contrast, marked differences were identified for the PAA-based formulation. Under identical test conditions, *C. auris* consistently showed substantially lower $\log_{10}$ reduction values than *C. albicans*. The most pronounced discrepancy was observed at 0.75% PAA with 5 min contact time, where *C. albicans* achieved a mean reduction of 5.09 ± 0.21 $\log_{10}$, fulfilling yeasticidal efficacy criteria ($\geq$4.0 $\log_{10}$ reduction), whereas *C. auris* reached only 1.88 ± 1.30 $\log_{10}$.

Comparative susceptibility of C. albicans *and* C. auris *to selected marketed products*

Testing of commercially available oxidative disinfectant products A–E confirmed that the susceptibility differences identified in the active substance screening translated into formulation-dependent efficacy differences under standardized product test conditions (Figure 2).

Marked differences between *C. albicans* and *C. auris* were observed for selected PAA-based formulations, whereas others showed robust activity against both organisms. The strongest susceptibility differences became apparent under conditions near the yeasticidal efficacy threshold, where inclusion of transitional test conditions enabled discrimination between surrogate and target-organism performance.

Products A and B demonstrated consistently high yeasticidal activity, achieving complete efficacy against *C. albicans* and all tested *C. auris* clades under the evaluated conditions, with no evidence of reduced *C. auris* susceptibility.

In contrast, relevant susceptibility gaps emerged for products C and D. For product C, the VAH-listed clean-condition application (1.0%, 5 min) achieved full yeasticidal efficacy against *C. albicans*, whereas efficacy against *C. auris* clade I remained below the required $\geq$4.0 $\log_{10}$ reduction threshold, indicating an increased RCAU relative to the surrogate organism.

Product	Conc. [%]	Contact time	*C. albicans*	*C. auris*	Δ
PAA	0.75	1 min	3.76 ± 0.55	1.05 ± 0.54 ***	–2.71
		5 min	5.09 ± 0.21	1.88 ± 1.3 ***	–3.21
		15 min	4.91 ± 0.52	4.7 ± 0.68	–0.21
DDAC	0.1	1 min	3.18 ± 0.41	3.5 ± 0.08	+0.32
		5 min	4.21 ± 0.03	4.2 ± 0.59	–0.01
		15 min	5.13 ± 0	5.15 ± 0.03	+0.02
IPA	50	15 sec	1.33 ± 0.39	3.91 ± 1.78	+2.58
		30 sec	3.12 ± 0.49	4.41 ± 1.07	+1.29
		60 sec	4.51 ± 0.57	5.01 ± 0.13	+0.5
GA	0.3	1 min	0.5 ± 0.4	4.44 ± 0.06	+3.94
		5 min	2.53 ± 0.61	5.46 ± 0.11	+2.93
		15 min	4.58 ± 0.44	5.46 ± 0.11	+0.88

Figure 1. Selected results obtained under defined experimental conditions illustrating the transition from insufficient to effective yeasticidal activity ($\geq$4.0 $\log_{10}$ reduction) and highlighting relevant susceptibility differences under identical exposure conditions. Mean $\log_{10}$ reduction values with standard deviation (SD) are shown. Red indicates substantially lower susceptibility of *C. auris* clade II compared with *C. albicans*. Asterisks indicate statistically significant differences compared with *C. albicans*: ***$P < 0.001$. Statistical comparisons were performed only for conditions in which *C. auris* showed markedly lower log reductions than *C. albicans*. PAA, peracetic acid; DDAC, didecyldimethylammonium chloride; IPA, isopropanol; GA, glutaraldehyde; Δ, difference in mean $\log_{10}$ reduction between *C. auris* and *C. albicans*.

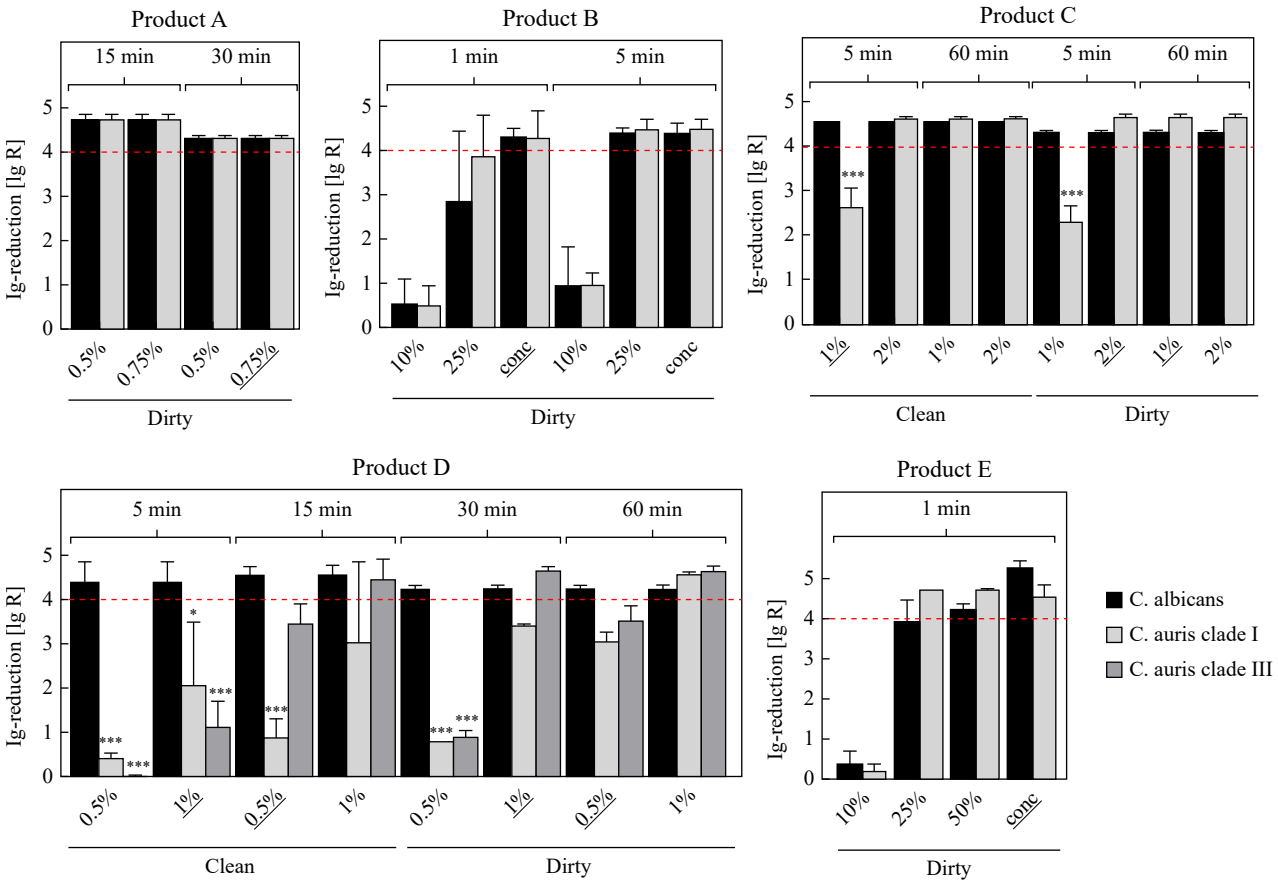

Figure 2. Comparative yeasticidal efficacy of selected commercially available oxidative disinfectant products against *C. albicans* and *C. auris* under defined quantitative suspension test conditions. Shown products include peracetic acid– and hydrogen peroxide–based formulations. Where applicable, selected test conditions were chosen to include the transition from insufficient to effective yeasticidal activity (≥4.0 $\log_{10}$ reduction; red dashed line), thereby enabling discrimination of relevant susceptibility differences between test organisms. Underlined conditions indicate VAH-listed application conditions (i.e. clean or dirty). Mean $\log_{10}$ reduction values are shown. Error bars indicate SDs. Asterisks indicate statistically significant differences compared to *C. albicans*: $^{*}P < 0.05$, $^{***}P < 0.001$. Statistical comparisons were performed only for conditions in which *C. auris* showed markedly lower log reductions than *C. albicans*. conc, concentrated (undiluted) product.

A more pronounced divergence was observed for product D. Under VAH-listed clean conditions, results for *C. albicans* fulfilled efficacy criteria, whereas both tested *C. auris* clades showed reduced susceptibility. Under dirty conditions, the discrepancy between the clades became even more evident: at 1.0%, insufficient efficacy was observed against clade I, whereas at 0.5%, both tested *C. auris* clades I and III remained below the required efficacy threshold despite adequate activity against *C. albicans*. Under these conditions, the persistence of viable *C. auris* indicates critical RCAU despite surrogate-based classification suggesting adequate efficacy.

In contrast, the hydrogen peroxide–containing oxidative formulation (product E) demonstrated consistently robust yeasticidal activity against *C. albicans* and *C. auris* clade I, with no relevant susceptibility gap.

Chlorine dioxide–based products F and G (Figure 3) demonstrated consistently high yeasticidal activity against *C. albicans* and all tested *C. auris* clades across the evaluated application conditions. Product F achieved robust efficacy against *C. auris* clades I, III, and IV without evidence of reduced activity compared with *C. albicans*. Similarly, product G achieved complete efficacy against all tested organisms, with *C. albicans* appearing less susceptible than *C. auris* under the evaluated conditions. No increased or critical RCAU of *C. auris* was observed for either chlorine dioxide–based formulation.

Discussion

The present study examined whether *C. albicans*, the established surrogate organism for yeasticidal disinfectant efficacy testing, adequately reflects the susceptibility of *C. auris* across different active substances, clades, and commercially formulated products. This question is clinically relevant given the global emergence of *C. auris* as a healthcare-associated pathogen and the increasing importance of effective environmental disinfection for transmission control [1–5].

A useful conceptual framework for interpreting these findings is provided by the recently introduced concept of RCAU [8].

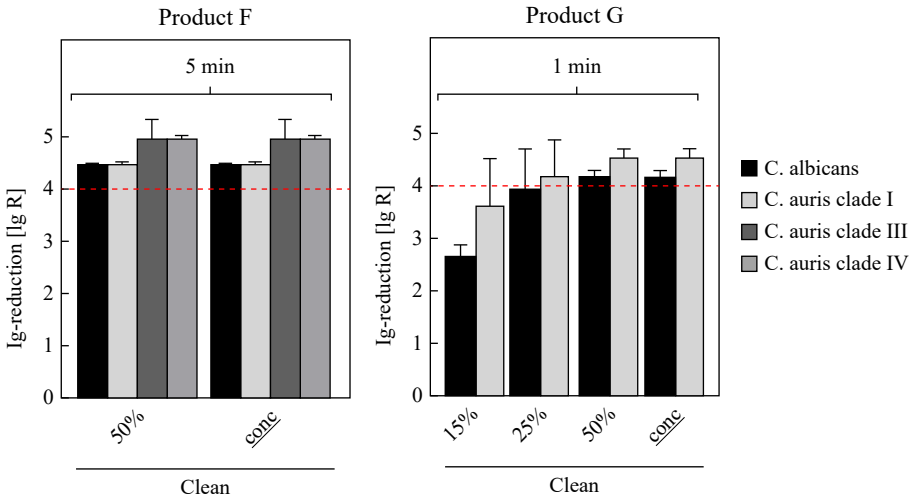

Figure 3. Comparative yeasticidal efficacy of selected commercially available chlorine dioxide—based disinfectant products (products F and G) against *C. albicans* and *C. auris* under defined quantitative suspension test conditions. Where applicable, selected test conditions were chosen to include the transition from insufficient to effective yeasticidal activity (≥4.0 $\log_{10}$ reduction; red dashed line), thereby enabling discrimination of relevant susceptibility differences between test organisms. Underlined conditions indicate VAH-listed application conditions. Mean $\log_{10}$ reduction values are shown. Error bars indicate SDs. conc, concentrated (undiluted) product.

Importantly, this concept does not support the notion of generalized disinfectant resistance in *C. auris*, but emphasizes that efficacy must be interpreted in relation to defined application conditions and clinically relevant residual survival. The present findings are fully consistent with this perspective. *C. auris* did not exhibit uniformly reduced susceptibility across disinfectant classes, but rather product- and clade-dependent differences.

This heterogeneity is supported by previous studies. Müller *et al.* [14] reported that *C. auris* can be equally or even more susceptible than *C. albicans* under standardized disinfectant test conditions, including EN 13624 suspension testing and EN 16615 surface disinfection testing. These findings support the adequacy of *C. albicans* as a surrogate organism in these settings. More recently, Lang *et al.* [13] demonstrated clade-dependent susceptibility differences, with clade I showing comparatively increased tolerance under selected conditions. Together, these studies suggest that susceptibility in *C. auris* cannot be regarded as a fixed species characteristic but must be interpreted in biological and methodological context.

The present data extend this concept by differentiating between intrinsic active substance susceptibility and efficacy of commercially formulated products under standardized test conditions. In the initial active substance screening, *C. auris* showed comparable or greater susceptibility than *C. albicans* for alcohol-based, aldehyde-based, and quaternary ammonium compound-based disinfectant exposures, whereas pronounced differences emerged for the oxidative PAA-based reference formulation.

At the product level, this translated into clearly divergent outcomes. Several oxidative products, including products A, B, and E—G, demonstrated robust efficacy against both *C. albicans* and all tested *C. auris* clades, confirming that surrogate-based testing remains adequate in most relevant contexts. In some instances, *C. albicans* even appeared slightly less susceptible than *C. auris*. In contrast, selected PAA-based formulations (products C and D) revealed relevant susceptibility gaps, including VAH-listed application conditions. Under these conditions, efficacy classification based on the surrogate organism would have indicated sufficient yeasticidal activity, while viable *C. auris* persisted. In RCAU terms, this represents a limitation of surrogate-based testing to conservatively predicted target-organism survival.

These findings underline that disinfectant efficacy cannot be inferred solely from active substance classification. Although pronounced susceptibility differences were observed with the PAA-based reference formulation during active substance screening, this pattern did not uniformly translate across all commercially formulated oxidative products. However, product E, containing both hydrogen peroxide and PAA, showed consistently robust efficacy, as did both chlorine dioxide—based products across all tested organisms. This aligns with recent literature demonstrating strong formulation dependence of disinfectant performance, including recent data indicating that efficacy against *C. auris* may be driven more strongly by formulation and concentration than by clade-specific resistance alone [9,13,21—23].

From a methodological perspective, the study design strengthens this interpretation. By separating intrinsic susceptibility screening from product testing and combining multiple *C. auris* clades with listed use conditions, the study distinguishes between organism-related susceptibility differences and formulation-dependent performance effects.

Additional data from clinical *C. auris* isolate collections and biocide-exposure models support this cautious interpretation. Clinical clade I isolates have shown variable biocide susceptibility profiles alongside antifungal resistance and virulence-associated characteristics, while experimental biocidal exposure has been reported to induce agent-specific adaptive shifts in both biocidal and antifungal susceptibility. These findings do not demonstrate a stable, generalized disinfectant-resistance phenotype, but they underline that isolate background and exposure history may influence susceptibility profiles and should be considered when interpreting product efficacy [10,11].

The practical implication is not a rejection of current surrogate-based testing frameworks. Established yeasticidal efficacy concepts using *C. albicans* remain justified. However, the present data indicate that this assumption may not hold universally across all product groups. For selected PAA-based formulations, biologically relevant susceptibility gaps may emerge that are not adequately captured by the surrogate organism.

Given the broad diversity of commercially available disinfectant formulations and the genetic heterogeneity of *C. auris*, comprehensive evaluation of all relevant product types and clades across every experimental setting was beyond the scope of a single comparative study. Nevertheless, the observed discrepancies under formally listed application conditions suggest that, while *C. albicans* remains an appropriate surrogate organism for most disinfectant products, expansion of surrogate-based efficacy testing to include *C. auris* may be justified for selected PAA-based formulations.

From a clinical perspective, the RCAU concept further emphasizes that disinfectant efficacy should ultimately be interpreted in relation to the actual organism, formulation, and use condition encountered in practice [8]. In settings involving persistent transmission, unusual environmental persistence, or concern regarding clinically relevant *C. auris* isolates, targeted susceptibility assessment of the implicated isolate against the disinfectant product in use may represent a rational infection prevention measure.

The present study represents an important step toward a more comprehensive understanding of *C. auris* susceptibility to disinfectants. To further strengthen the evidence base, complementary multi-centre laboratory investigations incorporating broader isolate collections and application-oriented test systems are currently in progress.

In conclusion, the present findings do not challenge the validity of current European disinfectant testing frameworks but highlight a relevant limitation in their application. Surrogate-based yeasticidal efficacy testing using *C. albicans* remains fundamentally sound. However, it may not be universally adequate across all disinfectant classes and biological contexts.

The data indicate that, under specific conditions, particularly in the presence of clade-dependent variability and for selected PAA-based formulations, surrogate organisms may not fully capture the susceptibility spectrum of *C. auris*.

A targeted inclusion of *C. auris* in selected testing scenarios therefore represents a rational and evidence-based refinement of existing methodologies, enabling a more accurate and context-sensitive assessment of disinfectant efficacy.

CRediT authorship contribution statement

K.-M. Mosel: Writing — review & editing, Investigation, Formal analysis, Data curation, Conceptualization. **A. Maharani:** Investigation, Data curation. **J. Mathew:** Investigation, Data curation. **M. Meckel:** Writing — review & editing, Validation. **A. Belitz:** Writing — review & editing, Validation. **F.A. Pitten:** Writing — review & editing, Validation, Conceptualization. **H. Gabriel:** Writing — review & editing, Conceptualization. **F.H.H. Brill:** Writing — review & editing, Validation, Conceptualization. **K. Konrat:** Writing — review & editing. **A.M. Richter:** Writing — review & editing. **J. Steinmann:** Writing — review & editing, Conceptualization. **A. Lang:** Writing — review & editing. **R. Beck:** Writing — review & editing, Investigation, Data curation. **B. Hornei:** Writing — review & editing, Conceptualization. **A. Dornaika:** Writing — review & editing. **A.D. Wollkopf:** Writing — review & editing, Conceptualization. **S. Engelhart:** Writing — review & editing, Validation, Formal analysis. **M. Exner:** Writing — review & editing. **C. Ilschner:** Writing — review & editing, Validation, Conceptualization. **N.T. Mutters:** Writing — review & editing, Validation, Supervision, Resources, Conceptualization. **J. Gebel:** Writing — review & editing, Validation, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **M. Rausch:** Writing — review & editing, Writing — original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics statement

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Conflict of interest statement

None declared.

Appendix A. Supplementary data

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