Review Article

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Candida Auris: The Emergence of a Multidrug-resistant Fungus

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Abstract

Candida auris has developed as a multidrug-resistant (MDR) fungal pathogen connected to medical care around the world. Due to its outbreak potential, antibiotic resistance, and high mortality, Candida auris infection has arisen as a significant problem in the care of patients admitted to ICUs in India. Candidemia caused by *C. auris* has been recorded from three continents since the initial report of ear-canal infection by this yeast in Japan in 2009, with a substantial number of cases from India. Some *C. auris* strains have higher minimum inhibitory concentrations (MICs) than amphotericin B and echinocandin compounds, while some *C. auris* strains are resistant to all antifungal medication classes. According to a comparison of European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute (CLSI) techniques, *C. auris* isolates exhibit strikingly comparable fluconazole resistance but a broad range of MICs for the other antifungal drug classes. The goal of this research is to learn more about curcumin's antifungal properties. This polyphenolic chemical has been used for medical, culinary, and other uses throughout Asia for centuries. Although curcumin has been shown to have antifungal properties, a current study reveals that curcumin works by disrupting the fungal cell wall.

Keywords: Candida auris; Multidrug resistance; Curcumin.

C. auris risk factors

C. auris infections have the same risk factors as other Candida species. This is usurprising, considering that many Candida species are opportunistic infections that are most commonly seen in severely sick and immunocompromised people. Elderly age, diabetes mellitus, recent surgery, the presence of an indwelling medical device (e.g., central venous catheter), an immunosuppressed state, hemodialysis, a neutropenic state, chronic renal disease, or the use of broad-spectrum antibiotics and/or antifungal drugs are all risk factors for *C. auris* infections.[1] An increase in *C. auris* colonizability was discovered in a study that retrospectively evaluated available patient data. An increase in C. auris colonization or infection was linked to diarrhea and the use of the broad-spectrum antibiotic tetracycline, as well as the second-generation tetracycline derivatives minocycline and tigecycline, according to research that retrospectively reviewed available patient data. These studies show that *C. auris* infections are linked to a wide range of risk factors.[2]

Antimicrobial resistance in C. auris

According to CLSI standards, all *Candida auris* isolates should be tested for antifungal susceptibility. Despite the fact that *C. auris* is

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usually multidrug resistant, antifungal resistance levels might vary greatly amongst isolates. There are presently no documented susceptibility breakpoints for *C. auris*. As a result, breakpoints are determined using data from closely related Candida species as well as expert opinion. At this moment, there is no evidence of a link between microbiologic breakpoints and clinical outcomes. As a result, the following information should be regarded as a broad guide rather than precise resistance breakpoints. Please keep in mind that an increased minimum inhibitory concentration (MIC) for an antifungal agent does not rule out its usage, especially if other antifungal treatments have failed to work for the patient. Many isolates are resistant to numerous kinds of medicine based on these MIC breakpoints. Some *C. auris* isolates from the United States have been reported to be resistant to all three antifungal medication classes.

We've also heard that pan-resistance has been discovered in other nations. In the United States, around 90% of *C. auris* isolates were resistant to fluconazole, about 30% to amphotericin B, and fewer than 5% to echinocandins. Multiple isolates from the same person may be included in these proportions, which may fluctuate as new isolates are examined.[3]

Table 1: MIC breakpoint of antifungal drugs and resistance.

Name of Drugs	MIC Range
FLU	≥32
VRC	N/A
AMB	≥2
AFG	≥ 4
CAS	≥ 2
MFG	≥ 4

FLU, Fluconazole; VRC, Voriconazole; AMB, Amphotericin B; AFG, Anidulafungin; CAS, Caspofungin; MFG, Micafungin (https://www.cdc.gov/fungal/candida-auris/c-auris- antifungal.html).

Ergosterol is the most abundant sterol in fungal membranes and is targeted by azoles (such as fluconazole) and polyenes (e.g., amphotericin B). Fluconazole, a first-line antifungal medicine, suppresses cellular ergosterol biosynthesis by targeting the fungal cytochrome P450-dependent enzyme lanosterol demethylase, which is required for ergosterol formation. In Candida species, ERG11 encodes lanosterol demethylase. Intriguingly, three hotspot mutations in Erg11 (Y132F, K143R, and F126L or VF125AL) have been discovered in fluconazole-resistant *C. auris* strains from various genetic clades. Although fluconazole and amphotericin B-resistant *C. auris* isolates are widespread, echinocandin-resistant isolates (e.g., caspofungin) are uncommon. In Candida species, FKS1 encodes the catalytic subunit of 1,3-beta-D-glucan synthase, which is required for cell wall formation and maintenance. *C. auris* isolates with an S639F mutation in Fks1 were resistant to caspofungin at human therapeutic dosages, but isolates with wild-type Fks1 were sensitive.[4]

- **Role of Melanin in fungus cell wall:** Melanin is a high-molecular-weight pigment that is negatively charged, hydrophobic, and insoluble in aqueous solutions, and it shields fungus from stressors while still allowing them to survive in the host.[5] The fungi produce melanin by two routes from 1,8-dihydroxynaphthalene (DHN) intermediate and from L-3, 4-dihydroxyphenylalanine (L-dopa).[6] Melanin synthesis aids fungal virulence, increases resilience to environmental stresses such as high temperatures, UV radiation, and toxins, and is crucial for invasion and spread. *c. neoformans* melanin, for example, has been related to the spread of yeast cells from the lungs to other organs and is known to alter the host's immunological response.[7]
- **Antifungal properties of curcumin:** Curcumin or diferuloylmethane (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) and other curcuminoids are the major phytochemicals found in the rhizome of Curcuma longa L. (Zingiberaceae family) known as turmeric.[8] Due to a diversity of biological actions, this polyphenolic molecule has piqued the interest of researchers all over the world. Due to the widespread traditional usage of turmeric in food items, several studies have been conducted to examine turmeric and curcumin in the context of preventing fungal spoilage and infections. The active component in turmeric may suppress melanin formation, according to 2012 research published in Phytotherapy Research. Curcumin is a chemical that inhibits the enzyme tyrosinase. This inhibits melanocytes' capacity to produce additional melanin.[9]

- Mannoproteins
- β-(1,3glucan), β-(1,6 glucan)
- Chitin

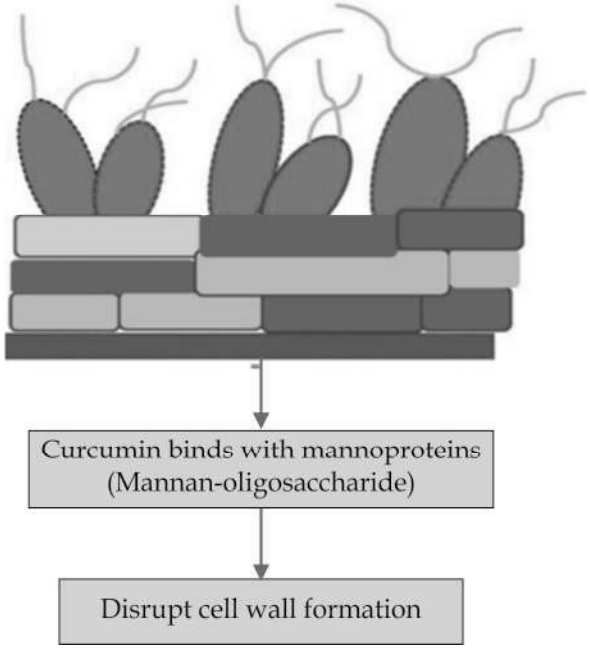

Fig: Schematic representation of candida cell wall and activity of curcumin.

Discussion

C. auris adaptability, genomic structure, virulence factors, and even techniques to treat the fungus in clinics are all being investigated. They've already made significant progress, but there's still a lot to learn about this fascinating organism's general biology, life cycle, other contributors to its genomic flexibility, and how to combat the yeast in patients. *Candida auris* shows some similarities to different species of candida. Some candida species contain melanin. If we treated *Candida auris* with curcumin, there is some possibility that curcumin inhibits the growth of candida auris because in humans, curcumin inhibits the production of melanin.

If this happens, then we can control the *candida auris* infection. Curcumin has been tested for a variety of biological activities, including antifungal activity against a variety of fungal infections, including *Paracoccidioides brasiliensis, Aspergillus niger, Sporothrix schenckii,* and Candida species. Because present antifungal medications have their limits, there has been a surge in interest in identifying new and more effective treatments, particularly those derived from natural sources.

Conclusion

The newly emerged multidrug resistant fungus, *candida auris* is a global health threat and has raised many questions in our minds. What were *C. auris's* initial environmental reservoirs? How did.

C. auris develop multidrug resistance? What allows *C. auris* to survive for lengthy periods of time in clinical settings? Finally, to battle infections caused by *C. auris* and other present and soon-to-be developing fungal diseases, we need to create innovative, safe, and effective antifungals and treatment techniques with a variety of pharmacological targets.

Future Prospective

Melanization might be a promising target for new antimicrobial treatments, so further research into melanin-inhibiting chemicals is needed in the future. Because the genome of *Candida auris* was recently decoded, information from genetic research is anticipated to provide more light on these findings.

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