

## The Rise of *Candida auris*: A Review of its Multidrug-Resistance Mechanisms and the Pipeline of Novel Antifungal Agent

Komal M. Yelonde\*, Nikita Mahale, Vaishnavi Deshmukh,  
*Shree Mahavir Education Society's Mahavir Institute of Pharmacy, Nashik, Maharashtra*

Dr. Vasim T. Pathan, *Department of Pharmaceutics*

Dr. Anil Jadhav, *Department of pharmacognosy*

Date of Submission: 12-05-2026

Date of Acceptance: 27-05-2026

### Abstract:-

Since 2009, there has been an increase in *Candida auris* infections from Eastern Asia to the Americas. This rise has led to many deaths and illnesses because treatments are often ineffective, and the fungus is resistant to several drugs. *C. auris* is one of the most concerning fungal pathogens related to healthcare in the 21st century. Genetic analysis shows that different groups of this organism have emerged simultaneously in various regions. Invasive infections and colonization mainly occur in patients in high-dependency environments. This situation raises concerns due to diverse antifungal resistance profiles and the spread of the fungus in units using different infection prevention measures. *C. auris* poses a significant threat in critical care medicine because of the increasing number of immunocompromised patients, with candidiasis being the leading cause of fungal infections. Since the first case was reported in Japan in 2009, infections have been documented in over 40 countries, with death rates between 30% and 60%. *C. auris* can also trigger outbreaks in healthcare settings, particularly in nursing homes for elderly patients, because it spreads easily through skin-to-skin contact.

**Keywords:-** *Candida auris*, *Candidozyma auris*, multidrug resistance, antifungal agents, echinocandins, novel therapeutics, biofilm, nosocomial infection, antifungal pipeline.

### I. Introduction:-

*Candida auris* is a newly emerged member of the *Candida/Clavispora* clade, first isolated in Japan in 2009 from the ear discharge of a female patient (5). The number of human fungal infections is rising at an alarming rate. These eukaryotic pathogens now infect billions of people around the world and kill more than 1.5 million people every year (6). The high death rates from invasive fungal

infections are similar to those from common bacterial and parasitic diseases like tuberculosis and malaria (6). About 90% of all deaths from fungal infections are caused by species of *Candida*, *Aspergillus*, or *Cryptococcus* (6). From its discovery in 2009 until June 2020, *C. auris* has attracted considerable attention from both clinical and basic science research fields (7).

*C. auris* distinguishes itself from other *Candida* species through three defining features: multidrug resistance, outbreak potential, and diagnostic ambiguity. It is often resistant to at least one, and often more than one, category of antifungal agents, resulting in clinicians having few effective treatment options (8). It is highly transmissible through environmental reservoirs and asymptomatic carriers, which boost its capability to cause prolonged and widespread outbreaks in critical care units. Adding to this multidrug resistance is the fact that it is often misidentified using standard diagnostic systems, thus being misidentified as other *Candida* species, potentially leading to inappropriate treatment. Such features require immediate consideration by infection control structures that have long been focused on bacterial pathogens (9, 10). *C. auris* is a new pathogen, and it may be misidentified and underreported because automated systems don't always get it right. This is because *C. auris* biochemical fingerprints haven't been added to many microbiology databases yet. *C. auris* has been incorrectly identified as other *Candida* species, *Rhodotorula glutinis*, and *Saccharomyces cerevisiae* in commercially available automated systems (11). Many clinical labs use RapID Yeast Plus (Remel, Thermo Fisher Scientific, Lenexa, KS), a commercial, manual, biochemical enzyme-based system, to find medically important yeasts (55).

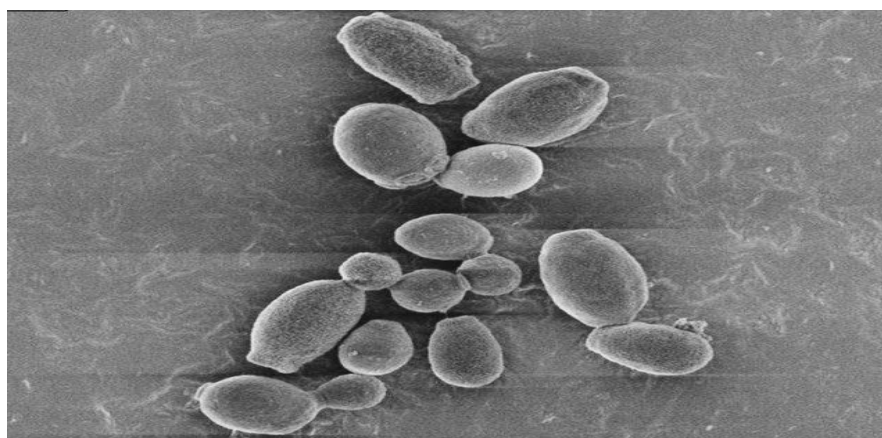


Figure 1 scanning electron microscopy of *Candida auris*

### 1.2 Objective and Scope of this Review

In this review, our aim is to give an exhaustive overview of the current state of knowledge regarding *C. auris* infections, emphasizing its resistance to multiple drugs and novel drugs for the treatment of fungal infections. We begin with a discussion of the distribution of this pathogen and its genetic variability worldwide. Next, we explore the mechanisms of resistance to azoles, polyenes, and echinocandins and the formation of biofilms. The final part of our paper will be devoted to the analysis of promising therapies, including novel drugs.

### II. The Global Epidemiology of *Candida auris*

Satoh et al. were the first to call *C. auris* a new pathogen in 2009 (12). It ideally grows at 37 °C, but also exhibits growth at 40–42 °C, albeit slowly (45, 50). A single isolate was first reported from the discharge of the external ear canal of a 70-year-old patient at Tokyo Metropolitan Geriatric Hospital (Tokyo, Japan). Detailed Phenotypic, chemotaxonomic, and phylogenetic analyses showed that the organism belonged to the *Candida* genus, and was closely related to less common species such as *C. haemulonii* and *C. pseudohaemulonii*. Subsequently, in South Korea, 15 patients suffering from chronic otitis media were found to be infected with unusual yeast isolates. These isolates were later confirmed through genomic sequencing to be *Candida auris*, and they were found to be clonally related (14).

Table 1 Global Clades of *Candida auris* with their geographic origin, year and features:

Clade	Geographic Origin	Year Identified	Key Features
Clade I	South Asia (India, Pakistan, Bangladesh)	2009 (retrospective to 2004)	<ul style="list-style-type: none"> <li>• Most Common clade globally</li> <li>• High Fluconazole resistance and moderate Amphotericin B resistance</li> <li>• Associated with large outbreaks</li> </ul>
Clade II	East Asia (Japan, South Korea)	1996 (retrospective), 2009 (formal)	<ul style="list-style-type: none"> <li>• Less virulent in animal models</li> <li>• Lower antifungal resistance (except fluconazole)</li> <li>• Often isolated from ear infections (not just bloodstream)</li> </ul>
Clade III	Africa (South Africa)	2012 (retrospective to 2005)	<ul style="list-style-type: none"> <li>• High Fluconazole resistance</li> <li>• Variable Amphotericin B susceptibility</li> <li>• Associated with neonatal outbreaks</li> </ul>
Clade IV	South America	2013	<ul style="list-style-type: none"> <li>• High Fluconazole and</li> </ul>

	(Brazil, Venezuela, Colombia)	(retrospective to 2010)	<ul style="list-style-type: none"> <li>Amphotericin B resistance</li> <li>Emerging Echinocandin resistance</li> <li>Associated with healthcare outbreaks in ICUs</li> </ul>
Clade V	Iran	2022	<ul style="list-style-type: none"> <li>Genetically distinct from other clades</li> <li>Lower overall resistance profile initially (but fluconazole-resistant)</li> </ul>
Clade VI	Singapore	2023	<ul style="list-style-type: none"> <li>Most recently identified clade</li> <li>Genetically distant from Clade I-V</li> </ul>

In subsequent years since its discovery, *Candida auris* infection cases have increasingly been reported in many geographical regions around the globe such as India, Pakistan, South Korea, Malaysia, South Africa, Oman, Kenya, Kuwait, Israel, United Arab Emirates, Saudi Arabia, China, Colombia, Venezuela, the USA, Russia, Canada, Panama, the UK, and other countries in Europe (50).

The fast spreading ability of the microorganism has seen it reported in dozens of countries around most continents (13, 15, 17).

### III. Unraveling the Multidrug-Resistance (MDR) Mechanisms of *C. auris*

#### 3.1. Intrinsic vs. Acquired Resistance: A Foundation for Pan-Resistance

Resistance mechanisms in *Candida auris* include intrinsic and acquired mechanisms. Intrinsic resistance is the natural property of the pathogen to withstand the presence of the antifungal agent regardless of previous exposure. In this case, it is mostly observed with fluconazole, where most *Candida auris* strains possess high minimum inhibitory concentrations (MICs) levels intrinsically. Acquired resistance occurs when genetic alterations take place following the pathogen's exposure to the drug. As a result, pan-resistance strains arise that are resistant to all three types of drugs: azoles, polyenes, and echinocandins (17).

#### 3.2 Resistance to Azoles

Azoles are the frontline drugs for most *Candida* species in systemic infections; nonetheless, due to the increased application of medicines, there is a constant emergence of resistance towards drugs (27). Over 90% of the clinical strains of *C. auris* is known to exhibit a high level of resistance to azole medications, especially fluconazole, while some types of *C. auris* strains exhibit a high degree of resistance to all three major antifungal classes (19). Azoles inhibit lanosterol 14 $\alpha$ -demethylase enzyme, an enzyme coded by the ERG11 gene, which plays a

vital role in ergosterol production. Azole resistance occurs in almost all *C. auris* strains (45). Point mutations within the ERG11 gene coding for lanosterol 14 $\alpha$ -demethylase result in amino acid changes, hence alteration in the structure of the target enzyme, decreasing its binding affinity to the azoles (18).

#### 3.3 Resistance to Polyenes (e.g., Amphotericin B)

Polyenes remain in clinical use due to the wide range of efficacy (echinocandins, first and second generation azoles) exhibited against pathogens from the genera *Candida*, *Aspergillus*, *Cryptococcus*, *Fusarium*, *Mucorales* (*Rhizopus* spp.), and endemic mycoses (*Histoplasma* spp.) (22). Amphotericin B (AmB) is fungicidal through direct binding to ergosterol present in the cell membrane, thus forming pores that cause cell death. However, several studies indicate that treatment of systemic mycoses with AmB caused by organisms, e.g., *Aspergillus terreus*, *Scedosporium* spp. and *Candida auris*, may not always be efficacious, mostly due to intrinsic or acquired resistance (21). AmB resistance is commonly mediated by mutations affecting ergosterol biosynthesis, especially ERG2 (C-8 sterol isomerase) and ERG3 (C-5 sterol desaturase). Mutations in these genes result in loss of function, preventing buildup of highly cytotoxic 14 $\alpha$ -methyl-3,6-diols which are accumulated as a result of AmB binding. Instead, the membrane gets saturated with non-specific sterols, which exhibit low affinity for AmB (23).

#### 3.4 Resistance to Echinocandins

The echinocandins (caspofungin, micafungin, anidulafungin) target the synthesis of the fungal cell wall component mediated by the enzyme  $\beta$ -(1,3)-D-glucan synthase (27). As of today, the recommendation is to use echinocandins as a primary treatment in cases of *C. auris* infection, with a relatively low number of isolates showing resistance (<5% worldwide). When the resistance

occurs, the selection of a proper treatment is very limited. The antifungal susceptibility testing by caspofungin was particularly difficult due to the appearance of Eagle effect (or paradoxical growth effect) by all isolates with the wild-type FKS1 allele at different intensities. The experiment involving 8 representative isolates aimed to determine if the Eagle effect leads to pharmacodynamic resistance in vivo using a murine model of invasive candidiasis. Except for the isolates carrying the S639F mutation, all isolates remained susceptible to caspofungin administered in a human therapeutic dose. These results demonstrate that only FKS1 mutant isolates show resistance to echinocandins (24). It should be mentioned that antifungal susceptibility testing of the *C. auris* isolates by the broth microdilution method should not be done or performed with caution. AFST was performed on a panel of 106 *C. auris* isolates obtained from Colombia (56 isolates), India (40 isolates), and the AR isolate bank (10 isolates). Four isolates out of 106 (3.8%) originating from India showed elevated MIC levels of caspofungin ( $\geq 4$  mg/liter at 24 h) and, hence, were presumed to be resistant to all tested echinocandins (ANF, CAS, MCF) (25).

#### IV. The Current Antifungal Arsenal and its Limitations

At present, the clinical guideline for the management of invasive candidiasis, even *C. auris*, suggests the use of echinocandins, namely caspofungin and micafungin. For *C. auris* strains that are confirmed to be susceptible to echinocandins, liposomal amphotericin B (L-AmB) can be considered; however, L-AmB is highly toxic (27). Combination of a highly dose echinocandin and L-AmB may be considered for isolates showing resistance to both classes of antifungals. Fluconazole should not be employed since its resistance among isolates is near universal. World-wide estimates suggest that over 300 million people suffer from severe fungal infections each year, causing over 1.5 million deaths annually. Of great concern, the prevalence of resistance to currently used antifungals has significantly increased, with some evidence indicating that over 10% of all *Candida* bloodstream isolates across the globe are resistant to fluconazole, a very common drug used for treatment. Thus, there is an urgent need to provide better access to novel antifungals, ensuring they are cheaper and safe at the same time (26).

##### 4.1 The Urgent Need for Novel Therapeutic Strategies

Considering the increased cases of MDR and PDR *C. auris* infections, the inefficiencies of currently available treatment options, and lengthy diagnostic procedures, there is a need for innovative antifungal drugs. The ideal antifungal drugs should have the following qualities: (1) a unique mode of action that circumvents resistance mechanisms, (2) ability to target biofilms, (3) oral bioavailability for use in step-down therapy and ambulatory care, (4) a good safety profile, and (5) activity against pan-resistant strains.

#### V. The Pipeline of Novel Antifungal Agents and Therapeutic Approaches

The antifungal pipeline of *C. auris* infections comprises several antifungal drugs, including rezafungin, ibrexafungerp (IBX), fosmanogepix, and T-2307 (arylamidine antifungal agent). The first drug is a prospective antifungal agent that emerged from anidulafungin and demonstrates significant in vitro antifungal activity towards *C. auris*, including echinocandin-resistant strains (28). The medication possesses a prolonged half-life, which allows weekly dosing of the medication. Clinical trials have demonstrated that rezafungin has a favorable toxicity profile with a low rate of adverse events. Conventional oral itraconazole capsules exhibit a bioavailability of about 55%, depending on whether the drug is consumed with meals, while its bioavailability is decreased in people with high stomach acidity (that is, those receiving acid suppression treatment). This condition prompted the creation of super-bioavailability-itraconazole or SUBA-itraconazole. IBX is a novel class of medications (antifungal terpenoids) utilizing a proven mode of action. As echinocandins, the drug inhibits the synthesis of 1,3- $\beta$ -d-glucan for antifungal effect. Nonetheless, in contrast to echinocandins, IBX is a triterpenoid enfumafungin derivative (28).

##### 5.1 Ibrexafungerp: First-in-Class Triterpenoid (Inhibits Glucan Synthase)

Ibrexafungerp (SCY-078 or MK-3118, Brexafemme) is a semisynthetic analog of the naturally occurring compound, enfumafungin, and represents the first drug in the triterpenoid class of antifungal agents. Ibrexafungerp exhibits wide-spectrum in vitro activity against various isolates of *Aspergillus* spp. and *Candida* isolates, including resistant strains such as *C. glabrata* and *C. auris*, exhibiting point mutations *fkf1* and *fkf2* conferring resistance to echinocandin antifungal drugs (30). Ibrexafungerp exhibits strong fungicidal action

against *Candida* spp. Both the triterpenoid class and the echinocandins share an analogous mechanism of action and inhibit the production of 1,3- $\beta$ -D-glucan by non-competitively inhibiting the enzyme 1,3- $\beta$ -D-glucan synthase complex. However, ibrexafungin belongs to a different class of drugs compared to echinocandins, with different structural and overlapping binding sites, resulting in minimal cross-resistance between the two different classes. In vitro activity studies of ibrexafungin were carried out using 16 clinical isolates of *C. auris* collected from countries including Germany, Japan, India, and South Korea, and a MIC<sub>90</sub> value of 1  $\mu$ g/mL was observed for ibrexafungin. (30, 32).

### 5.2 Fosmanogepix: First-in-Class Gwt1 Inhibitor (Disrupts Protein Anchoring)

Fosmanogepix (FMGX, PF-07842805, APX001, E1211) is a prodrug that is metabolized in vivo to the pharmacologically active metabolite manogepix (MGX, APX001A, E1210) via systemic phosphatases after administration. Manogepix is a novel anti-fungal compound that acts via inhibition of the fungal acyltransferase enzyme Gwt1, an integral part of the GPI-anchored protein maturation process (31). The enzyme Gwt1 is critical for the proper trafficking and attachment of mannoproteins to the plasma membrane and the cell wall. Inhibition of Gwt1 enzyme in *C. albicans* and *S. cerevisiae* has shown to alter maturation and localization of GPI-anchored mannoproteins. This drug demonstrates potent activity against several pathogenic yeasts, molds, and dimorphic fungi, including *Candida auris* and *Aspergillus fumigatus* resistant to azoles. Furthermore, the in vitro antifungal activity of manogepix has been validated in mice for experimental candidemia caused by *C. albicans*, *C. glabrata*, and *C. auris* (30, 31).

### 5.3 Rezafungin: Long-Acting Echinocandin

Rezafungin (SP3025 and CD101; Cidara Therapeutics, San Diego, CA, USA) is believed to be the first second-generation echinocandin drug, demonstrating improved PK/PD pharmacokinetic/pharmacodynamic profiles. Currently, two phase III clinical trials are conducted for rezafungin to study its effectiveness as a treatment of candidemia and other invasive candidiasis, as well as its ability to prevent IFD (33, 46). In contrast to most echinocandins, rezafungin demonstrates enhanced PK properties while avoiding hepatotoxicity due to reduced metabolism while maintaining the high efficacy of this class of drugs. In common with the rest of the echinocandin

class, the action of rezafungin includes the inhibition of  $\beta$ -1,3-D-glucan synthase, an enzyme in the cell wall of fungi (34). Similar to anidulafungin, rezafungin represents an analog with the same alkoxy triphenyl component but different modifications at the C5 ornithine hemiaminal of the echinocandin core – choline aminal ether. For example, in cases of resistant *Candida guilliermondii*, those drugs are not equally effective in vitro, taking longer and larger doses to achieve fungicidal effect (30, 33, 34).

## VI. Beyond Treatment: Prevention and Control in Healthcare Settings

For reducing the chances of spreading *C. auris* infection in acute care settings, healthcare personnel should apply both standard and contact precautions as advised by the CDC (35). After curing invasive infections, patients become carriers of these infections for a long time, hence, infection prevention measures must be applied at the time of treating this infection as well. If any patient with colonization or *Candida* infections is shifted from the health care facility to some other place, then it must be informed about this multiresistant organism (36).

Proper cleaning of the room occupied by the infected person is necessary using EPA-approved disinfectants, whose effectiveness is certified against fungal microorganisms (37). The risk of invasive infections due to *C. auris* will rise in the coming years because of the increasing number of co-morbidities in patients each year. According to one large UK outbreak, 2% chlorhexidine washcloths or 4% chlorhexidine solution was used to reduce skin shedding (37); however, despite such efforts, patients suffering from this infection continue to carry it in their body (38).

## VII. Future Perspectives

Experimental studies with mice have confirmed that *C. auris* is more transmissible and sometimes resistant when compared with other *Candida* species. However, one must understand that resistance does not always mean virulence. *C. auris* is another perfect example of new pathogens developing increased resistance. Climate change is likely playing a role in causing the appearance of this pathogen. The reason behind its success as a nosocomial pathogen lies in the fact that it can survive for a long time in the ICU. In order to counter this, it is essential to increase the development of antifungal drugs because of their limited number (40). In order to avoid infection,

health care institutions need to practice surveillance through monitoring and detection of the patients' medical history. For instance, in case where a patient is found to have contracted *C. auris* and later admitted again to the facility, doctors will be notified to take measures to prevent its transmission without having to go through the process of rescreening again. Moreover, the present SARS-CoV-2 outbreak creates an excellent environment for its proliferation, enabling it to become a hidden enemy for the COVID-19 population, with multiple cases of *C. auris* invasions reported from COVID-19 departments (41, 44).

### VIII. Conclusions

Echinocandins are now considered the drug of choice for treating *C. auris* infections since they are effective and safe, although their selection is based on the prevalence of azole resistance and varying sensitivity to amphotericin B (40). It is clear that the world is going through an epidemic period where some infectious diseases have become prevalent, while there is a lack of antifungal agents, which makes the control of fungal infections a pressing issue. Fungal infections occur less frequently compared to bacterial infections; hence, there are fewer antifungal agents available. The discovery of unique fungal pathways is vital for the development of new antifungal agents (42). However, the few antifungals available are being overused, abused, misused, and used for too long, resulting in antifungal resistance.

There are several areas of development and innovation in the research on nanoparticles as a solution to *C. auris* biofilms, and the following are some examples of recent developments. Targeted nanoparticles have been designed to possess targeting capabilities, and this can be achieved by modifying them with ligands or antibodies that recognize biofilm-specific molecules (43).

### References:-

- [1]. Osei Sekyere J. *Candida auris*: A systematic review and meta-analysis of current updates on an emerging multidrug-resistant pathogen. *MicrobiologyOpen*. 2018;7:e578. <https://doi.org/10.1002/mbo3.578>.
- [2]. Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, Johnson EM, Borman A, *Candida auris* Incident Management Team, Manuel R, Brown CS. 2018. *Candida auris*: a review of the literature. *Clin Microbiol Rev* 31:e00029-17. <https://doi.org/10.1128/CMR.00029-17>
- [3]. Cristina, M.L.; Spagnolo, A.M.; Sartini, M.; Carbone, A.; Oliva, M.; Schinca, E.; Boni, S.; Pontali, E. An Overview on *Candida auris* in Healthcare Settings. *J. Fungi* **2023**, *9*, 913. <https://doi.org/10.3390/jof9090913>
- [4]. Anuradha Chowdhary, Kusum Jain, Neeraj Chauhan. 2023. *Candida auris* Genetics and Emergence. *Annual Review Microbiology*. 77:583-602. <https://doi.org/10.1146/annurev-micro-032521-015858>
- [5]. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiol Immunol*. 2009;53(1):41–44. pmid:19161556.
- [6]. Brown GD, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. **2012**. Hidden killers: human fungal infections. *Sci. Transl. Med.* 4:165rv13 [Google Scholar].
- [7]. Du H, Bing J, Hu T, Ennis CL, Nobile CJ, Huang G (2020) *Candida auris*: Epidemiology, biology, antifungal resistance, and virulence. *PLoS Pathog* 16(10): e1008921. <https://doi.org/10.1371/journal.ppat.1008921>
- [8]. Hau, P.T.; Shiu, A.; Tam, E.W.; Chau, E.C.; Murillo, M.; Humer, E.; Po, W.W.; Yu, R.C.; Fung, J.; Seto, S.W.; et al. Diversity and Antifungal Susceptibilities of Yeasts from Mangroves in Hong Kong, China—A One Health Aspect. *J. Fungi* **2024**, *10*, 728. [Google Scholar].
- [9]. Akinbobola, A.B.; Kean, R.; Hanifi, S.M.; Quilliam, R.S. Environmental reservoirs of the drug-resistant pathogenic yeast *Candida auris*. *PLoS Pathog*. **2023**, *19*, e1011268. [Google Scholar].
- [10]. Tharp, B.; Zheng, R.; Bryak, G.; Litvintseva, A.P.; Hayden, M.K.; Chowdhary, A.; Thangamani, S. Role of microbiota in the skin colonisation of *Candida auris*. *Mosphere* **2023**, *8*, e00623-22. [Google Scholar].
- [11]. Snayd M, Dias F, Ryan RW, Clout D, Banach DB. 2018. Misidentification of *Candida auris* by RapID Yeast Plus, a Commercial, Biochemical Enzyme-Based Manual Rapid Identification System. *J Clin Microbiol* 56:10.1128/jcm.00080-18. <https://doi.org/10.1128/jcm.00080-18>
- [12]. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated

- from the external ear canal of an inpatient in a Japanese hospital. *Microbiol Immunol.* 2009;53:41–4.
- [13]. Rudramurthy SM, Chakrabarti A, Paul RA, Sood P, Kaur H, Capoor MR, et al. *Candida auris* candidaemia in Indian ICUs: analysis of risk factors. *J Antimicrob Chemother.* 2017;72:1794–801.
- [14]. Kim M-N, Shin JH, Sung H, Lee K, Kim E-C, Ryoo N, et al. *Candida haemulonii* and closely related species at 5 university hospitals in Korea: identification, antifungal susceptibility, and clinical features. *Clin Infect Dis.* 2009;48:e57–61.
- [15]. Magobo RE, Corcoran C, Seetharam S, Govender N, Naicker S. *Candida auris*: an emerging, azole-resistant pathogen causing candidemia in South Africa. *Int J Infect Dis.* 2014;21:215.
- [16]. Belkin A, Gazit Z, Keller N, Ben-Ami R, Wieder-Finesod A, Novikov A, et al. *Candida auris* infection leading to nosocomial transmission, Israel, 2017. *Emerg Infect Dis.* 2018;24:801.
- [17]. Shawn R. Lockhart. *Candida auris* and multidrug resistance: Defining the new normal; *Fungal Genetics and Biology*, Volume 131, 2019, 103243, ISSN 1087-1845, <https://doi.org/10.1016/j.fgb.2019.103243>
- [18]. Jacobs SE, Jacobs JL, Dennis EK, Taimur S, Rana M, Patel D, Gitman M, Patel G, Schaefer S, Iyer K, Moon J, Adams V, Lerner P, Walsh TJ, Zhu Y, Anower MR, Vaidya MM, Chaturvedi S, Chaturvedi V. 2022. *Candida auris* Pan-Drug-Resistant to Four Classes of Antifungal Agents. *Antimicrob Agents Chemother* 66:e00053-22. <https://doi.org/10.1128/aac.00053-22>
- [19]. Jangir, P., Kalra, S., Tanwar, S. and Bari, V.K. (2023), Azole resistance in *Candida auris*: mechanisms and combinatorial therapy. *APMIS*, 131: 442-462. <https://doi.org/10.1111/apm.13336>
- [20]. Carolus, H.; Pierson, S.; Lagrou, K.; Van Dijck, P. Amphotericin B and Other Polyenes—Discovery, Clinical Use, Mode of Action and Drug Resistance. *J. Fungi* 2020, 6, 321. <https://doi.org/10.3390/jof6040321>
- [21]. Cornely, O.A.; Vehreschild, J.J.; Ullmann, A.J. Is there a role for polyenes in treating invasive mycoses? *Curr. Opin. Infect. Dis.* 2006, 19, 565–570. [Google Scholar]
- [22]. Chandrasekar, P. Management of invasive fungal infections: A role for polyenes. *J. Antimicrob. Chemother.* 2011, 66, 457–465. [Google Scholar]
- [23]. Fenton, A., John, G.K. *Candida auris* Resistance Mechanisms to Amphotericin B Alternative Treatments Development. *Curr Clin Micro Rpt* 11, 166–176 (2024). <https://doi.org/10.1007/s40588-024-00233-w>
- [24]. Kordalewska M, Lee A, Park S, Berrio I Chodhary A, Zhao Y, Perlin DS. 2018. Understanding Echinocandin Resistance in the Emerging Pathogen *Candida auris*. *Antimicrob Agents Chemother* 62:10.1128/aac.00238-18. <https://doi.org/10.1128/aac.00238-18>
- [25]. K. E. Pristov, M. A. Ghannoum, Resistance of *Candida* to azoles and echinocandins worldwide, *Clinical Microbiology and Infection*. Volume 25, Issue 7, 2019, Pages 792-798; ISSN 11198-743X. <https://doi.org/10.1016/j.cmi.2019.03.028>
- [26]. Pooja Joshi, Archana Navale, Ajay Shelke and Muskan Patel. Exploring the arsenal of Novel Antifungal Drug Targets for Combating Fungal Infections. Bentham science Publication: *Current Pharmaceutical Biotechnology*. Vol. 26, Issue 13, 2025; Pages 2097-2110. <http://dx.doi.org/10.2174/0113892010304880240828075411>
- [27]. Nathan P. Wiederhold, The antifungal arsenal: alternative drugs and future targets, *International Journal of Antimicrobial Agents*. Volume 51, Issue 3, 2018; Pages 333-339; ISSN 0924-8579. <https://doi.org/10.1016/j.ijantimicag.2017.09.002>
- [28]. Gintjee, T.J.; Donnelley, M.A.; Thompson, G.R. Aspiring Antifungals: Review of Current Antifungal Pipeline Developments. *J. Fungi* 2020, 6, 28. <https://doi.org/10.3390/jof6010028>
- [29]. Ghannoum, M.; Arendrup, M.C.; Chaturvedi, V.P.; Lockhart, S.R.; McCormick, T.S.; Chaturvedi, S.; Berkow, E.L.; Juneja, D.; Tarai, B.; Azie, N.; et al. Ibrexafungerp: A Novel Oral Triterpenoid Antifungal in Development for the Treatment of *Candida auris* Infections. *Antibiotics* 2020, 9, 539. <https://doi.org/10.3390/antibiotics9090539>
- [30]. Espinel-Ingroff, A.; Wiederhold, N.P. A Mini-Review of In Vitro Data

- for *Candida* Species, Including *C. auris*, Isolated during Clinical Trials of Three New Antifungals: Fosmanogepix, Ibrexafungerp, and Rezafungin. *J. Fungi* **2024**, *10*, 362. <https://doi.org/10.3390/jof10050362>
- [31]. Shaw, K.J.; Ibrahim, A.S. Fosmanogepix: A Review of the First-in-Class Broad Spectrum Agent for the Treatment of Invasive Fungal Infections. *J. Fungi* **2020**, *6*, 239. <https://doi.org/10.3390/jof6040239>
- [32]. Tagirova L.I., Farvazova K.R., Valeeva D.R., Orlova M.D., Gubaidullin I.A., Tulyabaeva A.M., Abdulmanova A.R., Tryapko R.V., Shelyginsky D.A., Khanafieva A.R., Semenova N.G., Takiullin E.M. Reviewing the mechanism of action and results of clinical studies on the antifungal drug ibrexafungerp. *Obstetrics, Gynecology and Reproduction*. **2024**;18(2):232-245. (In Russ.) <https://doi.org/10.17749/2313-7347/ob.gyn.rep.2024.500>
- [33]. Hoenigl, M., Sprute, R., Egger, M. *et al.* The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin. *Drugs* **81**, 1703–1729 (2021). <https://doi.org/10.1007/s40265-021-01611-0>
- [34]. Garcia-Effron, G. Rezafungin—Mechanisms of Action, Susceptibility and Resistance: Similarities and Differences with the Other Echinocandins. *J. Fungi* **2020**, *6*, 262. <https://doi.org/10.3390/jof6040262>
- [35]. Cristina, M.L.; Spagnolo, A.M.; Sartini, M.; Carbone, A.; Oliva, M.; Schinca, E.; Boni, S.; Pontali, E. An Overview on *Candida auris* in Healthcare Settings. *J. Fungi* **2023**, *9*, 913. <https://doi.org/10.3390/jof9090913>
- [36]. Vallabhaneni, S.; Kallen, A.; Tsay, S.; Chow, N.; Welsh, R.; Kerins, J.; Kemble, S.K.; Pacilli, M.; Black, S.R.; Landon, E.; *et al.* Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus—United States, May 2013–August 2016. *Am. J. Transpl.* **2017**, *17*, 296–299. [Google Scholar].
- [37]. Nikki Kenters, Martin Kierman, Anuradha Chowdhary, David W. Denning, Javier Peman, Katja Saris, *et al.* Control of *Candida auris* in healthcare institutions: Outcome of an International Society for Antimicrobial Chemotherapy expert meeting, International Journal of Antimicrobial Agents; Volume 54, Issue 4, 2019; Pages 400-406; ISSN 0924-8579. <https://doi.org/10.1016/j.ijantimicag.2019.08.013>
- [38]. Ahmad, S., Asadzadeh, M. Strategies to Prevent Transmission of *Candida auris* in Healthcare Settings. *Curr Fungal Infect Rep* **17**, 36–48 (2023). <https://doi.org/10.1007/s12281-023-00451-7>
- [39]. Giacobbe, D. R., Magnasco, L., Sepulcri, C., Mikulska, M., Koehler, P., Cornely, O. A., & Bassetti, M. (2021). Recent advances and future perspectives in the pharmacological treatment of *Candida auris* infections. *Expert Review of Clinical Pharmacology*, *14*(10), 1205–1220. <https://doi.org/10.1080/17512433.2021.1949285>
- [40]. De Gaetano, S.; Midiri, A.; Mancuso, G.; Avola, M.G.; Biondo, C. *Candida auris* Outbreaks: Current Status and Future Perspectives. *Microorganisms* **2024**, *12*, 927. <https://doi.org/10.3390/microorganisms12050927>
- [41]. Garcia-Bustos, V.; Cabanero-Navalon, M.D.; Ruiz-Saurí, A.; Ruiz-Gaitán, A.C.; Salavert, M.; Tormo, M.Á.; Pemán, J. What Do We Know about *Candida auris*? State of the Art, Knowledge Gaps, and Future Directions. *Microorganisms* **2021**, *9*, 2177. <https://doi.org/10.3390/microorganisms9102177>
- [42]. Ganeshkumar, A.; Muthuselvam, M.; Lima, P.M.N.d.; Rajaram, R.; Junqueira, J.C. Current Perspectives of Antifungal Therapy: A Special Focus on *Candida auris*. *J. Fungi* **2024**, *10*, 408. <https://doi.org/10.3390/jof10060408>
- [43]. Fayed, B. Nanoparticles in the battle against *Candida auris* biofilms: current advances and future prospects. *Drug Deliv. and Transl. Res.* **15**, 1496–1512 (2025). <https://doi.org/10.1007/s13346-024-01749-w>
- [44]. Zoi, V., Skoulatou, M., Vassilikopoulos, T. *et al.* Managing *Candida auris* in dialysis units: challenges, strategies, and future directions. *Int Urol Nephrol* **57**, 4141–4153 (2025). <https://doi.org/10.1007/s11255-025-04600-4>
- [45]. Karoline Kristina Kemmerich, Suelen Andreia Rossi, Joao Nobrega de Almeida Junior, Arnaldo Lopes Colombo and Lysangela Ronalte Alves. Understanding *Candidozyma (candida) auris*: genomic

- evolution, antifungal resistance and the growing challenges in global infection control. Volume 75, Issue 3, 2026. <https://doi.org/10.1099/jmm.0.002135>
- [47]. Guillermo Quindos, Carolina Garcia-Vidal, Xabier Martin-Martitequi, Rafael Zaragoza. Antifungal activity of rezafungin in invasive candidiasis: From bench to bed, *Revista Iberoamericana de Micología*, 2026, ISSN 1130-1406.
- [48]. <https://doi.org/10.1016/j.riam.2026.02.001>
- [49]. atoh, K., Makimura, K., Hasumi, Y., Nishiyama, Y., Uchida, K. and Yamaguchi, H. (2009), *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiology and Immunology*, 53: 41-44. <https://doi.org/10.1111/j.1348-0421.2008.00083.x>
- [50]. Shawn R. Lockhart, Kizee A. Etienne, Snigdha Vallabhaneni, et al. Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses, *Clinical Infectious Diseases*, Volume 64, Issue 2, 15 January 2017, Pages 134–140, <https://doi.org/10.1093/cid/ciw691>
- [51]. Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, Johnson EM, Borman A; *Candida auris* Incident Management Team; Manuel R, Brown CS. *Candida auris*: a Review of the Literature. *Clin Microbiol Rev.* 2017 Nov 15;31(1):e00029-17. DOI: 10.1128/CMR.00029-17. PMID: 29142078; PMCID: PMC5740969.
- [52]. Centers for Disease Control and Prevention. Tracking *Candida auris*. Updated March 20, 2024. Accessed April 3, 2026. <https://www.cdc.gov/candida-auris/tracking-c-auris/index.html>
- [53]. Johanna Rhodes, Matthew C. Fisher. Global epidemiology of emerging *Candida auris*. *Current Opinion in Microbiology*, Volume 52, 2019; Pages 84-89. ISSN 1369-5274. <https://doi.org/10.1016/j.mib.2019.05.008>
- [54]. Lone SA, Ahmad A. *Candida auris*—the growing menace to global health. *Mycoses*. 2019;62:620–637. <https://doi.org/10.1111/myc.12904>
- [55]. Cortegiani, A., Misseri, G., Fasciana, T. *et al.* Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. *J intensive care* 6, 69 (2018). <https://doi.org/10.1186/s40560-018-0342-4>
- [56]. Chakrabarti A., & Singh S. (2020). Multidrug-resistant *Candida auris*: An epidemiological review. *Expert Review of Anti-Infective Therapy*, 18(6), 551-562.
- [57]. <https://doi.org/10.1080/14787210.2020.1750368>
- [58]. Micelly-Moreno, J.; Barreto-Santamaría, A.; Arévalo-Pinzón, G.; Firacative, C.; Gómez, B.L.; Escandón, P.; Patarroyo, M.A.; Muñoz, J.E. Therapeutic Use of the Antimicrobial Peptide PNR20 to Resolve Disseminated Candidiasis in a Murine Model. *J. Fungi* 2023, 9, 1149.
- [59]. <https://doi.org/10.3390/jof9121149> [CrossRef]