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ASPECTS OF THE FEATURES OF CHALLENGES OF ANTIFUNGAL RESISTANCE, ISSUES OF MYCOTOXICOLOGY, MYCOECOLOGY AND PROBLEMS OF BIOLOGICAL SAFETY IN GENERAL

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სოკოს საწინააღმდეგო რეზისტენტობის გამოწვევების თავისებურებები, მიკოტოქსიკოლოგიის ასპექტები, მიკოეკოლოგიის საკითხები და ბიოლოგიური უსაფრთხოების პრობლემები

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რეზიუმე

სტატია მიმოიხილავს Candida-ს სახეობებთან დაკავშირებულ ძირითად ასპექტებს, მათ შორის მათ კლინიკურ მნიშვნელობას, სოკოს საწინააღმდეგო რეზისტენტობის მექანიზმებს, მიკოტოქსიკოლოგიურ რისკებს, გავრცელებასა და ბიოუსაფრთხოების გამოწვევებს. Candida სოკოები ოპორტუნისტული პათოგენების მნიშვნელოვან ჯგუფს წარმოადგენენ, რომლებსაც შეუძლიათ იმუნოკომპრომეტირებულ პირებში ინფექციების ფართო სპექტრის გამოწვევა. კანდიდას სხვადასხვა გარემოში ადაპტაციის მექანიზმების და ბიო წარმოქმნის უნარის შესწავლა მნიშვნელოვანია პათოგენეზის გასაგებად და ეფექტური თერაპიული სტრატეგიების შემუშავებისთვის. გარდა ამისა, სოკოს საწინააღმდეგო რეზისტენტობა სულ უფრო აქტუალური საზოგადოებრივი ჯანმრთელობის პრობლემა ხდება, რაც ანტიმიკრობული თერაპიის ახალ მიდგომებს მოითხოვს. მიკოტოქსიკოლოგიური კვლევები მიუთითებს კანდიდას ზოგიერთი მეტაბოლიტის პოტენციურ ტოქსიკურობაზე და მათი მონიტორინგის საჭიროებაზე.

Introduction: Fungi of the genus Candida play a significant role in the human microbiome and environment, however, under certain conditions they can become pathogenic. Candida infections are an important problem of modern medicine, especially in connection with the growth of the population of immunocompromised patients. The increase in cases of invasive candidiasis is associated with the widespread use of antibiotics, immunosuppressive therapy, and an increase in the number of medical interventions, such as the installation of catheters and the implantation of prostheses. An important feature of Candida is the ability to form biofilms, which significantly complicate therapy, reducing the effectiveness of antimycotics and increasing the risk of recurrent infections.

Candida species represent a significant problem in medical and environmental mycology because of their pathogenic potential, resistance to antifungal drugs, and effects on human health. In this discourse, key aspects of Candida-related problems are discussed, with emphasis on resistance to antifungal drugs, production of mycotoxins, ecological interactions, and biosafety problems. The growing prevalence of Candida strains with multiple drug resistance, including Candida auris, has increased the urgency of developing new therapeutic strategies. In addition, the role of mycotoxins in the pathogenicity of fungi and interactions with the host remains the most important area of research. The alarming growth of antifungal resistance, especially in Candida auris and other species of Candida, other than albicans, has complicated the treatment regimen, which required the development of new antifungal drugs and

alternative therapeutic strategies. The molecular mechanisms causing resistance, such as overexpression of the efflux pump, biofilm formation and genetic mutations in the target sites of drugs, are studied in detail. In addition, the potential role of mycotoxins in the pathogenicity of Candida, modulation of virulence and evasion of the immune response of the host remains insufficiently studied, but a critically important aspect of fungal infections.

Aim of the research was to study and analyze the features of challenges of antifungal resistance, issues of mycotoxicology, mycoecology and problems of biological safety in general.

Methodology: The material of the article was the revised data from scientific publications, which were processed, analyzed, overviewed and reviewed by generalization and systematization. Research studies are based on a review/overview assessment of the development of critical visibility and overlook of the modern scientific literature. Use the following databases (for extensive literature searches to identify the features of challenges of antifungal resistance, issues of mycotoxicology, mycoecology and problems of biological safety in general): PubMed, Web of Science, Clinical key, Tomson Reuters, Google Scholar, Cochrane Library, and Elsevier Foundations.

Results and discussion. The study showed that Candida infections are of growing global concern due to increasing antifungal resistance, high mortality rates in invasive infections, and the emergence of multidrug-resistant species. Clinical isolates showed a significant shift from Candida albicans to non-albicans species such as C. auris and C. glabrata, which demonstrated high resistance to azole and echinocandin antifungals.

Formulation was a key feature observed in resistant Candida strains, contributing to increased drug tolerance and persistent infections. In hospitalized patients, candidemia was strongly associated with prolonged intensive care unit stay, immunosuppression, and prior antibiotic use. Molecular analysis identified genetic mutations in Candida strains associated with resistance, particularly in ergosterol biosynthesis and echinocandin target genes. One of the primary drivers of resistance is the widespread and often indiscriminate use of antifungal drugs in both human medicine and agriculture. The extensive application of triazoles in crop protection has fostered cross-resistance in environmental fungi like *Aspergillus fumigatus*, which subsequently infect immunocompromised individuals. Similarly, prolonged antifungal therapy in clinical settings, especially among patients with hematologic malignancies or organ transplants, has led to the selection of multidrug-resistant fungal strains. Diagnostic challenges further compound the problem, as current laboratory methods may lack the sensitivity or speed to detect resistance early in the course of infection, leading to delays in the initiation of effective therapy.

The epidemiology of antifungal resistance is also evolving, with global travel, hospital outbreaks, and climate change contributing to the spread of resistant fungi across regions. Notably, *Candida auris* has demonstrated the ability to persist on surfaces and resist standard disinfectants, causing nosocomial outbreaks that are difficult to contain. This emphasizes the need for improved infection control practices and robust surveillance systems to track the emergence and dissemination of resistant strains.

Addressing antifungal resistance requires an integrative approach involving advancements in diagnostics, antifungal stewardship programs, the development of novel therapeutic agents, and a deeper understanding of fungal biology. Emerging strategies include the use of combination therapies, repurposing of existing drugs, immunotherapeutics, and targeting resistance mechanisms through molecular inhibitors. Moreover, interdisciplinary collaboration between microbiologists, clinicians, pharmacologists, and policymakers is essential to formulate comprehensive responses to this growing threat. Antifungal resistance poses significant clinical and public health challenges that demand urgent attention. Its complexity lies not only in the diverse mechanisms and species involved but also in the

interconnectedness of medical, agricultural, and environmental factors. A proactive, globally coordinated strategy encompassing surveillance, research, innovation, and education is vital to curb the spread of resistance and safeguard the effectiveness of antifungal therapies for future generations.

Studies have shown that some Candida species can produce toxic metabolites that promote cellular injury and inflammation. These metabolites have been implicated in disrupting epithelial integrity, facilitating fungal invasion and promoting persistent infections. Additionally, interactions between Candida and other mycotoxin-producing fungi, such as Aspergillus and Fusarium, may result in synergistic effects that enhance fungal pathogenicity. Co-infections with mycotoxin-producing molds and Candida are associated with severe clinical outcomes, particularly in immunocompromised patients. One of the significant issues in mycotoxicology and Candida infections is the impact of fungal toxins on antifungal resistance. Mycotoxins can alter fungal stress response pathways, potentially inducing tolerance to antifungal drugs. Several studies suggest that exposure to environmental mycotoxins may promote genetic and epigenetic changes in Candida, leading to increased virulence and resistance. In addition, mycotoxin contamination of food and pharmaceutical products raises concerns about indirect effects that may impact fungal colonization and infection severity.

Conclusion: Mycotoxicology studies indicate that fungal secondary metabolites may play a role in modulating Candida virulence, immune evasion, and antifungal resistance. Understanding these interactions is essential for developing targeted therapeutic interventions and preventing adverse health effects of fungal toxins. The ecological presence of Candida in both natural and built environments highlights its ability to persist in diverse settings. Monitoring Candida reservoirs, particularly in hospital and industrial settings, is critical to preventing contamination and reducing the risk of infections. Environmental factors, including pollution and climate change, may further influence the pathogenic potential of Candida species, requiring ongoing research into their ecological adaptation.Biosecurity concerns, particularly in healthcare settings, require stricter infection control measures, improved hygiene protocols, and the development of antifungal-resistant materials to reduce the risk of nosocomial infections. Preventive strategies, including routine monitoring of high-risk patients, biofilm-targeted therapies, and potential vaccine development, are essential to minimize the burden of Candida-associated disease.

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SUMMARY

The article reviews key aspects related to Candida fungi, including their clinical significance, mechanisms of antifungal resistance, mycotoxicological risks, ecological prevalence, and biosafety challenges. Candida fungi are an important group of opportunistic pathogens that can cause a wide range of infections in immunocompromised hosts. Studying the mechanisms of Candida adaptation to various environments and their ability to form biofilms is important for understanding the pathogenesis and developing effective therapeutic strategies. In addition, antifungal resistance is becoming an increasingly pressing public health problem requiring new approaches in antimicrobial therapy. Studies of mycotoxicological aspects indicate the potential toxicity of some Candida metabolites and the need for their monitoring.

Keywords: Antifungal resistance, mycotoxicology, mycoecology, biological safety.