WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 8.025
Volume 14, Issue 6, 318-351 Review Article ISSN 2278 – 4357

A REVIEW ON PHARMACOLOGICAL EVALUATION OF INDOLE DERIVATIVES FOR ANTIFUNGAL THERAPY

Anuj Kumar Sharma*, Preeti Anand and Robin Singh

Dept. of Pharmacy, IIMT College of Medical Sciences, IIMT University, 'O' pocket Ganga Nagar Mawana Road Meerut Uttar Pradesh 250001.

Article Received on
08 April 2025,

Revised on 28 April 2025,
Accepted on 18 May 2025

DOI: 10.20959/wjpps20256-29963

***Corresponding Author**
Anuj Kumar Sharma
Dept. of Pharmacy, IIMT College of Medical Sciences, IIMT University, 'O' pocket Ganga Nagar Mawana Road Meerut Uttar Pradesh 250001.

ABSTRACT

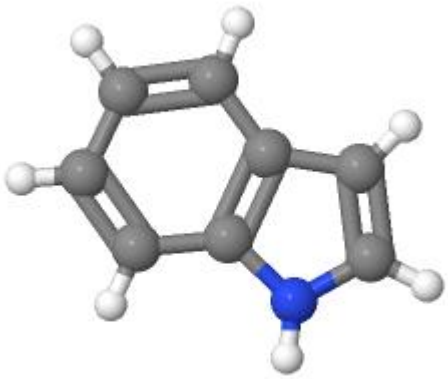
Indole derivatives have garnered significant attention in the field of medicinal chemistry due to their diverse pharmacological activities, including potent antifungal properties. This review focuses on the pharmacological evaluation of indole-based compounds as potential antifungal agents. The article summarizes the synthesis of various indole derivatives and their structural modifications aimed at enhancing antifungal efficacy. It highlights the mechanisms of action, including the inhibition of key fungal enzymes, disruption of cell membrane integrity, and interference with fungal cell wall biosynthesis. Additionally, the review provides an overview of in vitro and in vivo studies, examining their spectrum of activity against common pathogenic fungi, such as *Candida*, *Aspergillus*, and *Cryptococcus* species. The pharmacokinetic properties, toxicity profiles, and challenges in translating these compounds into clinical applications are also discussed. By evaluating the latest advancements, this review aims to provide insights into the potential of indole derivatives as a promising class of antifungal agents for future therapeutic development.

KEYWORDS-: Indole derivatives, Antifungal therapy, Medicinal chemistry, Synthetic strategies

1. INTRODUCTION

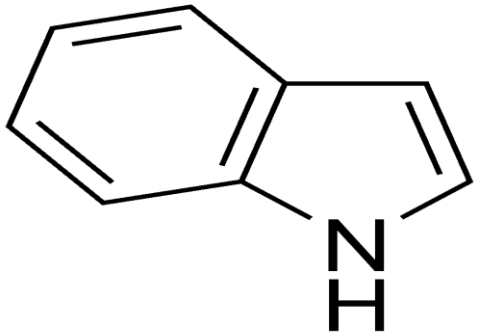
Indoles compounds possess a wide range of biological activities such as antimicrobial, antifungal and anti-inflammatory activities. As far as medicinal chemistry is concerned, the indole ring is important as it is the basic structure of a number of biologically active

medicines. Indoles have been found to be effective against different fungi, even the more serious pathogens like *C. albicans*.[1][2] Research shows that halogenated indole compounds are equally important because they can potentially increase the already existing antifungal potency and that the change of some structural parameters of these compounds will lead to better therapeutic value against fungal infections.[1] Indole compounds are of utmost importance these days in view of the rising problem of antifungal resistance to most commonly used drugs which is actually a problem of advanced stage when fungi cause serious infections. Azole compounds, which are known to have an indole structure, also have been gaining popularity due to their effectiveness in systemic candidiasis and other infections.[3][2] Moreover, through further research, increased development of these compounds may lead to more effective treatment for existing resistant strains of fungi.[3][4]



In the case of the increased dangers of fungal infections, the emergence of recurrent infections, and the simultaneous increase of resistance to antimycotic drugs, they cannot be stressed enough. Fungal infections, especially in patients with weak immunity, are highly hazardous which contributes to high morbidity and mortality rates.[4] The conventional antifungal agents used in practice include azoles, echinocandins, and polyenes with azoles being the most prominent due to their favorable pharmacokinetics and broad activity spectrum.[5][6] However, the increasing resistance of Candida albicans and other pathogenic fungi to these agents underscores the need to constantly to seek new antifungal compounds. Other novel approaches, such as drug repurposing and changing the structure of existing compounds, are being advanced to combat resistant strains.[4][5] For example, azoles are essential in the fight against resistant strains; however, their fungistatic nature often leads to the development of resistance.[5][6] Hence, the development of new indole derivatives that

pose different mechanisms of action might offer solutions to treat this urgent public health concern.[5] Indole derivatives are known for their wide range of biological activities rendering them an important group of compounds in medicinal chemistry. Its overarching bicyclic aromatic framework permits several substitutions and modifications that may profoundly change their biological functions.[7] There remains much interest in the synthesis and functionality of indole derivatives owing to their relevance in pharmaceuticals, especially for antifungal and antimicrobial applications.



Structure of indole moiet

2. Synthetic routes for developing indole-based antifungal compounds

Several methods have been reported to develop indole derivatives possessing antifungal activities. Jain et al. described the synthesis of N-oxidized indole derivatives by a reaction with oxalyl chloride followed by derivatization with aromatic amines to yield compounds that showed enhanced antimicrobial activities.[8] Xu and Fan also described the synthesis of new indole-based benzotriazine derivatives and their significant antifungal activities against phytopathogenic fungi.[9] This synergistically bolsters the application of indole derivatives in managing plant pathogenic fungi, which are incredibly detrimental to agriculture. Most of these routes rely on electrophilic substitution reactions and cyclization. Ölgen et al. synthesized N-alkylated indole-2- and -3-carboxamide derivatives and evaluated their antimicrobial activities, showing that even simple modifications can yield substantial changes in biological activities.[10] They further demonstrated that such structural modifications of the indole core have practical implications on the efficacy of these compounds against various pathogens.

Structural modifications for enhanced activity

It has been noted that the addition of functional groups in the 3-position of the indole ring improves the antifungal and antimicrobial properties. The 1H-indole-2,3-dione derivatives have shown positive in vitro results against Mycobacterium tuberculosis, suggesting that strategic substituent placement enhances pharmacological effects.[11] Banerjee's research focuses on the significance of indoles because their derivatives have anti-cancer activities, exhibit broad-spectrum antimicrobial activity, and many other biological functions.[12] There are other studies highlighting the influence of the indole nitrogen substituents on the compound's metabolic stability, receptor binding, and other factors.[13],[14] Some studies identify certain indole derivatives as antioxidants and associate specific structural elements with those activities, which shows the increasing need for rational design in indole-based drugs presented below in table 1.[15] Recent studies showed that modifications in indole-3-acetamido-polyamines reveal antibiotic-adjuvant activity, which suggests that adding extra groups to the derivatives increases their antibacterial effectiveness.[16] Thus, the constant development of synthetic strategies based on multifunctionalization of the indole core is essential to unlock the full therapeutic value of these compounds.

Table 1: Impact of structural modifications on the biological activity of indole derivatives, Enhancing their therapeutic properties.

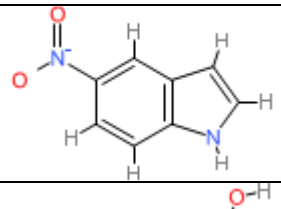
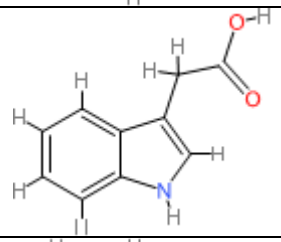
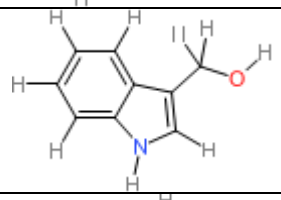
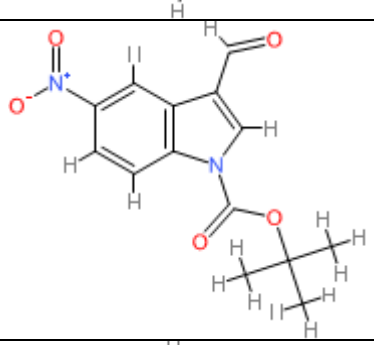
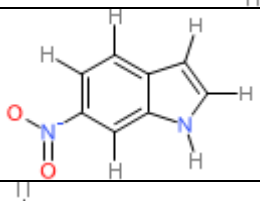
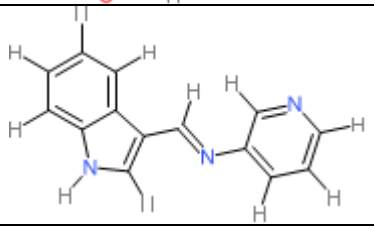
Indole Derivative	Functional Group Modification	Effect	Biological Activity	References
Indole-2,3-dione derivatives	Substituents at 3-position	Enhanced antifungal and antimicrobial activity	Effective against M. tuberculosis	[17]
Indole derivatives	Various nitrogen substitutions	Improved metabolic stability, receptor binding	Broad-spectrum antimicrobial activity	[18]
Indole antioxidants	Presence of antioxidant motifs	Antioxidant activity	Protective against oxidative stress	[19]
Indole-3-acetamido-polyamines	Extra groups (acetamido)	Increased antibiotic-adjuvant activity	Enhanced antibacterial effects	[20]

3. Pharmacological properties of indole derivatives

Indole derivatives exhibit diverse compounds that demonstrate remarkable and broad antifungal capabilities.Reasonable cell functions like the synthesis of enzymes and proteins as well as the integrity of the cell wall is critically important for fungi. Synthetic indole derivates, as well as other antifungals, tend to showcase mild to severe efficacy on fungal pathogens like Aspergillus flavus, and even more for Candida albicans. Some even had potent properties marked in the studies performed.[21],[22],[23] For instance, while performing the evaluation of minimum inhibition concentrations (MIC), indole derivates had emerged every time as the strongest contender for the Fungus pathogens with very few exceptions.[24],[25] Recently, indoles have been highlighted with immense potential and severe attention span due to the significant strain of fungi that does indeed get affected by it and has given promising results, where its value is set high against the extremely active indole strains.[26],[27] Those substituents like the 3-indolyl derivates do boost the membrane interaction with enzymes that perform the critical functions for cell metabolism and help slash down the survivable life of fungi, do provide severe results on the structure if not on the enzymes themselves. Indoles show great potential of ultrapathogenic species found, where utmost focus is placed on the structural Sasson indole derivatives along with other features exhibiting the supreme biological activity Table 2. below summarizes various Indole derivatives along with their associated biological activities.

The indole nucleus serves as a principal scaffold in the majority of the synthetic pathways, which offers derivatives with activity against diverse fungal pathogens, even those which are refractory to Candida and Aspergillus strains.[28],[29] Some of the Pharmacological profiles like solubility and stability are also included in the design of these compounds to maximize their application in clinical settings.[30],[31] The electronic characteristics of substituents have been linked with their antifungal activity potential in previous research.[32],[33] Therefore, advanced techniques such as molecular docking along with SAR could speed the discovery process of lead compounds designed to treat stubborn fungal infections. The persistent development of resistant fungal strains has driven researchers to study the potential of combining indole derivatives with existing antifungal drugs in a synergistic manner. This complements traditional antifungal action while possibly reducing dosages and minimizing side effects.[34],[35] This type of research focusing on combination therapies using indole derivatives may prove useful in solving the changes in resistance mechanisms to fungal infections and renewing the effectiveness of current antifungal treatments.

Table 2: Summarizes various Indole derivatives along with their associated biological activities.

Derivative Name	Biological Activity	Structure	References
Nitroindole	Antimycobacterial, Antifungal, Antiparasitic,		[36],[37]
Indole-3-acetic Acid	Anticancer, Antioxidant, Antibacterial		[38]
Indole-3-carbinol	Anti-inflammatory, Antioxidant, Antimicrobial		[39],[40]
5-Nitroindole	Antibacterial, Antifungal, Antiviral		[41],[42]
6-Nitroindole	Antimycobacterial, Antiviral, Antifungal		[43][44]
(1H-Indol-3-ylmethylene)-pyridin-3-yl-amine	Anticancer, Anti-inflammatory, Antimicrobial		[45],[46]

4. Bioavailability

Research on the pharmacokinetics and bioavailability of indole derivatives is of particular interest due to their various therapeutic applications, especially in cancer, antimicrobial, and anti-inflammation medicine. Optimizing the clinical value of these drugs requires understanding the absorption, distribution, metabolism, excretion (ADME) processes concerning these compounds and their derivatives.

4.1 Absorption

Absorption is a crucial step in the bioavailability of indole derivatives and there characteristics are not constant across different compounds. According to the review by Sakinala et al.[47] some indole derivatives have near 100% bioavailability following oral administration and about 80-90% bioavailability through rectal administration. These values suggest that indole compounds overcome gastrointestinal obstacles because of their high oral bioavailability, which vouches for passive diffusion driven by their lipophilic nature.[48] Moreover, in silico research indicates that numerous indole derivatives meet Lipinski's rule of five concerning absorption criteria, having optimal molecular descriptors for favorable absorption.[49] Factors such as cleavage, dissolution, molecular volume, and chemical stability affect the absorption rate, as well as the constructive changes to the compounds, which increase these factors and improve the therapeutic effectiveness.[50]

4.2 Distribution

The bio distribution of indole derivatives in the body depends on their physicochemical properties, including lipophilicity and protein binding affinity.Usually, more lipophilic compounds tend to to be distributed widely across organs and tissues which is an important factor for drugs meant for the central nervous system (CNS). Indole derivatives like vincristine and vinblastine have been reported to penetrate the blood-brain barrier which suggests serious CNS penetration.[51] Distribution profiling is often carried out by using predictive algorithms that take into consideration blood-brain barrier permeability, binding to the tissues, and volume of distribution, giving an indication of possible therapeutic achievements.[52] Moreover, in silico tools such as Swiss ADME provide robust predictive datasets that evaluate these parameters at the preliminary step of drug development,[53] supporting indole derivatives with appropriate distribution metrics.[54]

5.3 Metabolism activity

Metabolic studies of indole derivatives show that the biotransformation pathways which are quite intricate occur predominantly in the liver and are mediated by cytochrome P450 enzymes.These “-omic” metabolic processes have the potential to either activate prodrugs or deactivate unsafe substances.[55] The metabolism of indole derivatives within the organism may considerably influence the pharmacological activity and safety, as metabolism may yield ineffective compounds, while accumulating metabolites may increase toxicity.[56] Recent studies have assessed some of the specific indole derivatives for metabolic stability using in

vivo and in vitro models showing that some modifications can maintain active concentrations of the drug without flooding the metabolic pathway.[57] Predictive modeling helps in knowing the possible metabolic removal pathways of indole derivatives and helps in designing structures that have less adverse metabolic effects.[58]

5.4 Excretion

The total lifespan of excretion is one of the major factors plasma concentration persists until elimination. Indole derivatives are mainly excreted via the kidneys, so the hydrophobicity of the compounds is one of the most important characteristics determining excretion efficiency.[59] Compounds with low water solubility require biotransformation in the liver to yield increased polar metabolites that are readily removed.Assessing renal clearance rates revealed that some indole derivatives, particularly those used for anticancer therapies, have excretion profiles that are advantageous with respect to systemic exposure and potential side effects.[60] It is well-known in pharmacodynamics that one needs to account for routes of excretion and the need for bioactivity at the points of interest to avoid toxic effects on the organism.[61]

5.6 Drug-Drug interactions

By default, the diverse spectrum of biological activities of indole derivatives makes them susceptible to drug-drug interactions (DDIs). These interactions may arise through changes to the metabolic pathways, competition for enzymatic sites, or with displacement from plasma protein binding sites, thus greatly altering the pharmacokinetic parameters of combination therapies.[62] For example, the syndrome e of vincristine and vinblastine suffers from common metabolic pathways, which together delay drug clearance and produce increased toxicity when other drugs, like those that act on cytochrome P450 enzymes, are used.[63] Moreover, in silico studies have been very useful in evaluating possible DDIs by simulating several binding scenarios and resultant pharmacokinetic interactions, which is critical for safe coexistence of multiple drugs.[64] With knowledge of these interactions, researchers and clinicians can readily anticipate adverse effects and efficacy outcomes for indole derivative treatment schemes, diagrammatic representation of indole derivative mechanism is illustrated below in Fig 1.[65]

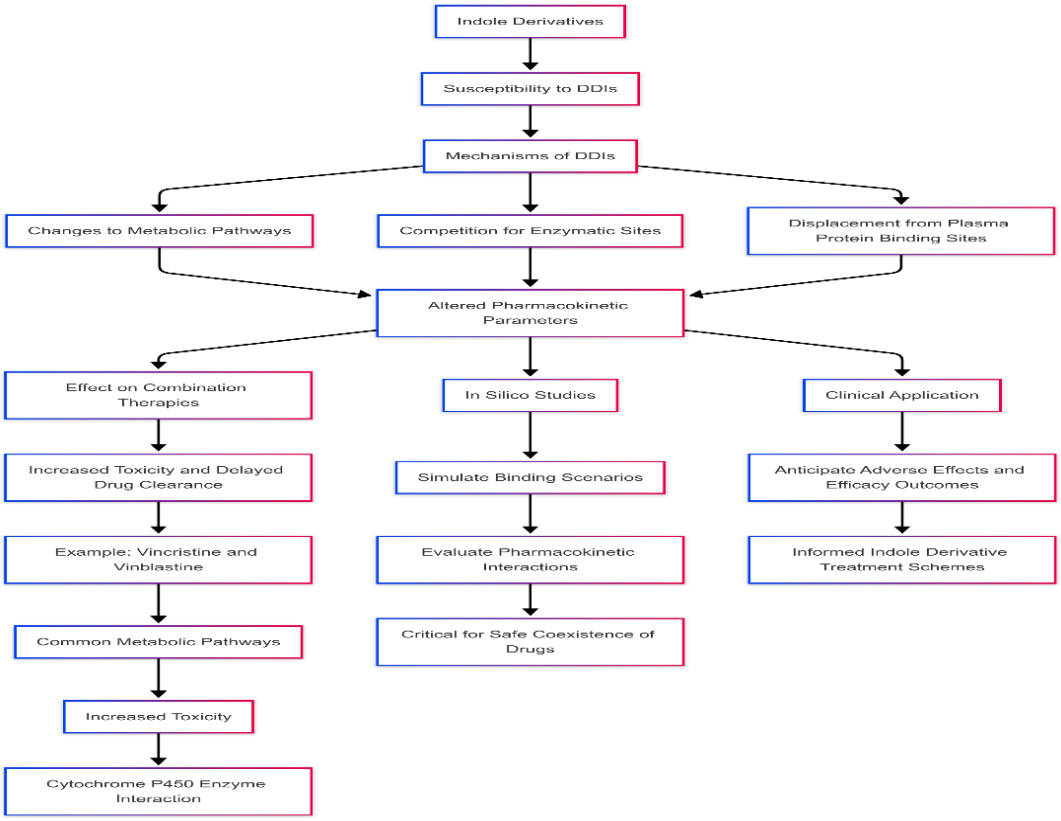


Fig. 1: Diagrammatic representation of indole derivative mechanism.

5. Toxicity and Safety profiles of indole derivatives

Indole Derivatives are a heterogenuous class of compounds which have been greatly studied due to their important biological actions such as anticancer activity, antiinflammatory and antimicrobial activities.Nonetheless, the secondary metabolites in question have numerous associated health risks, which require additional focus. The toxicity of indole derivatives is quite diverse and depends upon the chemical structure, specific substituents, and some therapeutic compounds that demonstrate elevated toxicity at higher concentrations. A case in point would be some derivatives that are known to cause oxidative stress and inflammation, possibly leading to renal and cardiovascular complications if maintained at certain excess levels.[66]

These properties of indoles might complicate their use in therapeutic contexts. Some indole derivatives, such as indole-3-acetic acid, possess positive agricultural uses and antipathogenic properties, but at the same time can also show some degree of toxic activity.[67] This dichotomy emphasizes the need to formulate an adequate balance between therapeutic promises and risks of safety regarding indole derivatives. The difference between acute and chronic toxic effects has been documented, defining acute exposure as an instantaneous

response with an almost immediate violent reaction, while chronic exposure is defined as a more subdued range of effects that includes potential malignancy.[68]

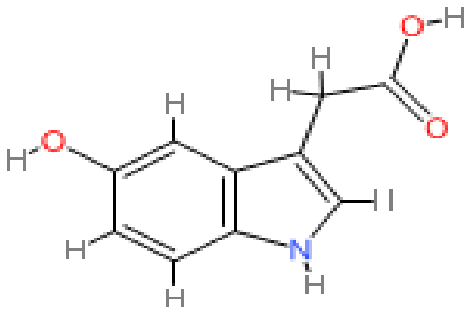


Fig. 2: Indole-3-acetic acid.

5.1 Acute and Chronic toxicity studies

Study of acute toxicity forms an integral part of the safety evaluation of indole derivatives.Several indole alkaloids exhibit varying acute toxicity within rodents and may even prove to be lethal at higher doses.[69] For example, the possibility of toxicity is bound to 1 mg/kg and exceeds 5000 mg/kg. This further highlights the need to study effects on a dose-reliant system.[70] In another research, the Alstonia scholaris-derived alkaloids showed no notable difference below 300mg/kg body weight; however, the underlying toxicology was equally elusive and called for further histological assessments.[71]

Chronic exposure studies are also needed for indole derivatives to determine their long term impact in terms of their potential mutagenicity and carcinogenicity. Protracted exposure to some of the indole derivatives has been connected to alterations in metabolism and cell function hinting a more profound nature which disturbs homeostasis.[7] The indole degradation metabolic byproducts that can result from microbial interaction further add to the complexity of the toxicity framework, as these metabolites can also produce unwanted biological impacts.[73]

7. Ailments and Hurdles

The pains and complications associated with indole are directly linked to the consequences resulting from the pharmacological attention set to them. As an example, some Indole derivatives appear to be useful anti-fungal agents through the selective inhibition of cyclooxygenases; however, they may lead to gastrointestinal disturbances and liver dysfunction with chronic use. It is noted that some indole-imidazolidine derivatives showed useful anti-fungal activity, yet their toxicological profile, in particular levels of cytotoxicity,

alters their value for clinical usefulness. Also, the diverse structural features of Indole derivatives lead to different biological activities. Indole derivatives demonstrate varying biological properties due to changes in complexity, such as changes in efficacy and toxicity, due to the modification of the indole nucleus, which is a reason to perform thorough structure-activity relationship SAR studies. Further, these facts demonstrate that designing new therapeutic compounds requires balancing therapeutic and harmful effects that limit the scope of clinical use.[74]

7.1 Obstacles to a clinical approach

Gaining perspective into barriers related to patients is important for the mitigation of clinical trial participation as well as the adoption of new therapies within clinical practice. Literature suggests that patients face gaps that result in them not being able to participate in clinical trials fully. For example, McKinney et al. explain that educational policies help overcome the gaps by offering patients crucial information and fostering patient participation through engaging them in the clinical trial processes.[75] Moreover, several other public perceptions regarding research trials also have a bearing on the level of participation, especially with regard to marginalized communities. Guerra et al. point out the systemic representation issues in cancer clinical trials and how they affect participation as critical.[76] Additionally, lack of technology could lower patient participation and compliance levels towards treatment regimens. Limited health technological resources can seriously discourage potential participants, especially in underprivileged areas, as shown by Storholm et al., pointing to the need for targeted access policies in these regions aimed at increasing participation levels.[77] Another view comes from Presseau et al. who argue that a participant's comprehension of the benefits and risks of treatment limits activities that are needed to attain the goals of the clinical trial. Healthcare providers, beyond factors related to the patient, are still faced with a unique set of barriers which challenge the incorporation of clinical evaluations into practice. From above, one major concern is the application of clinical guidelines into practice frameworks; for instance, physicians frequently struggle with the use of research within the Context of their clinical setting.[78] Curran et al. underline the guideline compliance variability associated with clinical practice inconsistency and its associated components.[79] Fischer et al.'s observation that mere lack of communication has, however, led the providers to fail to receive guidance makes compliance worse; that is why, as they argue, appropriate strategies make barriers disappear when applied thoughtfully disseminated information.[80]

Other examples of these barriers include organizational ones within the healthcare setting, especially related to the workflows, such as disruption of work or lack of teamwork across disciplines, severely hampers the effectiveness of clinical practices.[81] For example, Landis-Lewis et al. show how relatively simple sustention of health data through information technology is retarded by poor organization with rampant ignorance of adequate training for the personnel which greatly impedes provider participation.[82] As noted by Parks et al., absence of supportive interdisciplinary teams proves problematic for achieving desirable clinical outcomes, particularly in specialized care services for older patients.[83] So thus, these clinicians are often bound to work below the standard and ideal outcome level. Developing an overlapping cooperative network among healthcare providers top enable efficient communication aimed at eliminating the barriers is therefore important.

7.2 Formulation and Delivery challenges

Translating clinical research into practice results in an added layer of difficulty due to the formulation and delivery of clinical interventions. Stages of change within established clinical practices frameworks tend to be more difficult with the implementation of sophisticated tools such as Magnetic Resonance Imaging (MRI). For instance, application of MRI protocols for velopharyngeal function has been shown to face hurdles due to the accompanying provider's steep learning curve (Mason, 2002).[84] Moreover, the inadequate trained staff capable of operating such technologies often becomes a barrier to applying them in a clinical setting. In addition, the unavailability of certain equipment and supplies greatly decreases the effectiveness of novel treatment implementations. Abdrabalrasol et al. reported that training health care professionals in the provision of relevant tools was feasible making them readily adaptable in practice.[85] Research carried out by Ellis et al. has shown that physiotherapists acknowledge cost and training barriers that restrict the utilization of ultrasound imaging as clinically mandated instrumentation.[86] Hence, camouflaging the infrastructure triad of the technology denominators, logistics, and cost to the clinical purpose enhances maximizing translation efforts.

7.3 Knowledge Gaps and Ongoing Education

Dissemination of information and ongoing education amongst health care system professionals such as medical practitioners, physician assistants, and clinicians for peripheral care providers equate in priority with all components of clinical governance.Not comprehending new treatment approaches can decrease the possibility of healthcare providers

accepting new clinical guidelines and methods. Dmitriew and Ohle's study shows that a lack of training or misinformation can hinder the use of clinical decision support tools.[87][88] In the same way, Hoebes and Ashipala demonstrate how insufficient instructional materials for clinical teaching create knowledge deficits which impact the quality of care delivered to patients.[89] Additionally, the exclusion of patient education in clinical activities often neglects relevant knowledge transfer and clinical practice impacts patient care results at a deeper level.[90]

8. New indole derivatives in development as antifungal agents

The development of new indole derivatives as antifungal agents is an area of significant interest in contemporary medicinal chemistry. Indole compounds have demonstrated considerable potential against various fungal pathogens due to their structural diversity and ability to interact with specific biological targets. Recent studies emphasize the antifungal efficacy of modified indole derivatives. For instance, Shirinzadeh et al. explored new indole derivatives that include 1,2,4-triazole illustrated below in Figure 1, and found them to exhibit potent antifungal activity against multiple strains, particularly Candida krusei.[91] This aligns with findings reported by Bai et al., who characterized 3-Indolyl-3-hydroxy oxindole derivatives, noting that halogen-substituted indoles possess remarkable antifungal properties, which correlate with the structural optimization of the compounds.[92] Additionally, there is evidence that combining indole with other heterocycles, such as thiadiazoles, enhances antifungal effectiveness. He et al. have shown that novel indole derivatives containing 1,3,4-thiadiazole exhibit significant antifungal activity against plant pathogenic fungi, which support the hypothesis that integrating diverse heterocyclic components can enhance the biological activity of indole derivatives.[93]

Expanding on this theme, some researchers have initiated efforts to synthesize 4H-thiadiazolo4,5-bindole hybrids as potential antifungal agents. These hybrids demonstrated promising antifungal activities against various fungal strains, leveraging the thiadiazole framework's beneficial interactions in biological systems.[94] Furthermore, structural modifications to existing indole frameworks have produced a range of derivatives that show potential against resistant fungal strains, particularly in the context of systemic candidiasis, as highlighted by Sarı and Kart, who developed indole-azole derivatives.[95] Moreover, research led by Pagniez et al. has introduced 1,2,4-triazole-indole hybrid molecules, which present a new class of antifungal agents with demonstrated effectiveness against Aspergillus and

various Candida species.[96] Their study indicates that incorporating both indole and triazole structures facilitates interaction with fungal enzymes vital for growth, enhancing the overall antifungal activity. In addition to structural modifications, computational modeling has been increasingly used to predict and improve the efficacy of these compounds. The docking studies associated with these novel derivatives suggest a targeted approach can lead to more effective antifungal treatments, as demonstrated in prior assessments investigating the molecular interactions between these indole derivatives and their fungal targets.[97][98]

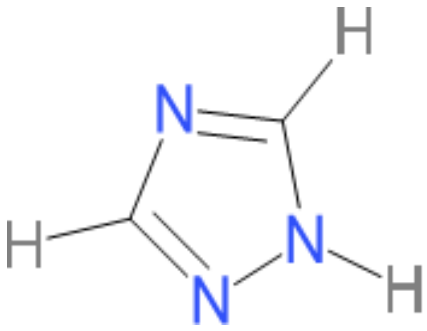


Fig. 3: 1,2,4-triazole.

8.1 Advances in Drug Design and Targeting

Indole derivatives are emerging as crucial components in drug design, particularly in the development of antifungal agents. The versatility of the indole scaffold stems from its rich biological activities and the ability to modulate various physiological pathways, making it a favorable candidate in modern medicinal chemistry. Recent literature confirms that indole derivatives exhibit significant antifungal properties. Notably, Kumar et al. emphasize that several indole-containing drugs, such as Indomethacin and Oxypertine, have been developed over the years, showcasing their effectiveness against both bacterial and fungal infections.[99] This is supported by findings from Mo et al., who explore the broader therapeutic applications of indole derivatives, including their roles in infectious disease management.[100] Their review highlights indole derivatives' adaptability, providing a scaffold for various modifications that enhance biological activity. Specific examples of successful synthesis and biological evaluation of indole derivatives demonstrate their antifungal potential. For instance, the synthesis of 1-(3-indoly)-3-aryl-2-propen-1-one oxime ethers and their subsequent testing showcased their efficacy against various fungal pathogens such as Botrytis cinerea and Anthracnose.[101] Moreover, the investigation by Kurmi et al. revealed an indole derivative with notable antifungal activity against Candida species, further validating the potential of indole structures in combating fungal infections.[102] The structure-activity

relationship (SAR) studies presented by Kumar et al. elucidate how specific modifications to the indole ring can influence antifungal effectiveness, indicating that tailored modifications can enhance biological activity.[103] Furthermore, molecular docking studies have been employed to predict the interactions of indole derivatives with fungal targets. Kumar et al. demonstrated that specific electronic properties of indole derivatives, such as dipole moment, play a critical role in their antifungal activity.[104] This computational approach is crucial for guiding drug design by allowing researchers to identify promising candidates before extensive synthesis and testing. The structural diversity afforded by indole derivatives also lends itself to the development of innovative compounds through combinatorial approaches. The synthesis of indole-triazole conjugates, as explored by Berdzik et al., has yielded compounds that display remarkable antibacterial and antifungal properties, marking a progressive step in drug discovery from this scaffold.[105] Such advancements are pivotal in addressing the rising challenge of antifungal resistance, particularly in immunocompromised populations where drug resistance among Candida species poses a significant health risk.[106]

9. Combination therapy potential

The existing literature articulates that combination therapies involving azole antifungal drugs, like fluconazole or itraconazole, along with indole derivatives can significantly improve the inhibition of fungi that exhibit resistance to standard treatments. Shrestha et al. delineated the effectiveness of combining azoles with various novel compounds, which produced synergistic interactions leading to enhanced antifungal activity against resistant strains of Candida albicans.[107] Similarly, Ahmad et al. described the synergistic action of certain cyclized chalcone derivatives with fluconazole against both susceptible and resistant strains of C. albicans.[108] Such findings suggest that harnessing the unique properties of indole derivatives in combination with existing antifungals could effectively circumvent issues of resistance. Moreover, several studies have specifically highlighted the antifungal potential of indole derivatives. For instance, bis-indolylmethane derivatives exhibit promising antifungal activities, showing potential as effective agents or in combination with other fungicides like azoles.[109] This is crucial as the development of fungicides that maintain efficacy against resistant pathogens is of paramount importance in clinical settings. The emergence of indole-linked triazole derivatives has also been demonstrated to enhance the therapeutic landscape, with studies indicating improved antifungal activity through structural modifications that combine the indole scaffold with triazole functionalities.[110][111]

10. Evaluation models of indole derivatives for antifungal activity

10.1 Broth Microdilution Technique: Standardization by CLSI and EUCAST

Over the past years, the research of indole derivatives as new candidates for the treatment of fungal infection has been increasingly focused, which may be closely related to the fact that indole derivatives possess a wide variety of biological activities. Their antifungal activity has been mostly tested using the broth microdilution method, standardized by Clinical and Laboratory Standards Institute (CLSI) or EUCAST protocols.

Some researches demonstrate the potential antifungal activities of certain indole derivatives. For instance, El-Sayed et al. isolated a novel potent antifungal metabolite produced by Bacillus toyonensis 6-methoxy-1H-indole-2-carboxylic acid that demonstrated strong inhibitory activity toward Candida albicans, pointing to its potential usefulness in antifungal treatments.[112] Similarly, Han et al. reported new thiochromanone analogues with an indole moiety and investigated their antifungal activity using the broth microdilution technique. According to their results, potential antifungal activities were observed against C. neoformans and C. albicans.[113]

The bioactivity of indole derivatives frequently requires structural modification to improve their potency. Sarı et al. showed that azole indole derivatives were effectively antifungal agents, particularly against fluconazole resistant C. tropicalis.[114] In reason of the flourishing resistant fungal strains that are being found in clinic, one of the strategic approaches is the introduction of azole moieties into the indole nucleus.

Recent studies have confirmed the involvement of indole derivatives in antifungal therapy and a general consensus among researchers has been formed towards its potential. Bai et al. tested halogen substituted indole-ring compounds, reporting increased antifungal activity, and supporting previous observations of structure-activity relationship.[115] Reported are Sofan et al. reinforced this trend with these derivatives exhibiting good efficacy against bacteria and fungi, which further highlights the flexibility of the indole scaffold for medicinal purposes.[116]

10.1.2 CLSI Guidelines

The CLSI furnishes recommendations on antifungal susceptibility testing in two documents, M27 (yeasts) and M38 (non-yeast molds). Key features include:

- Medium: RPMI 1640, containing 0.2% glucose and buffered with MOPS to pH 7.0.

- Preparation of inoculum: Normalized to 0.5 × 10^3 – 2.5 × 10^3 cells per mL, and for molds 0.4 × 10^4 – 5 × 10^4 conidia per mL.
- Incubation: Usually at 35 degree centigrade for 24 to 48 hours, depending on the organism.
- MIC: Macrodilution method (the broth microdilution method also can be applied) showing the lowest concentration without visible growth in terms of visual evaluation.[117][118]

10.1.3 EUCAST Guidelines

- The EUCAST method is similar to CLSI, however with some key differences:
- Medium: RPMI 1640 containing 2% glucose, pH 7.0 buffered.
- Inoculum of Biofilm Formation: The higher densities of initial inoculum (2 × 10^5–5 × 10^5 CFU/mL) were used for both the yeasts and molds.[119]
- Microdilution Plates A flat-bottomed plate is suggested for ease of measuring optical density.
- Incubation: At 35°C for 24 hours, in the case of yeasts and 48 hours, or longer, in the case of molds if necessary for more amounts.
- MIC Assay:Reading of optical density at 530 nm; the MIC is the lowest concentration giving a specified reduction in growth, e.g., ≥50% with azoles).[120]

10.2 Biofilm Inhibition Assays

Biofilm inhibiton assay are also performed for the indole derivatives to evaluate its antifungal effect, especially on Candida albicans because it is a pathogen that possess capability to form biofilm. These models also serve as screens for the discovery of compounds with antifungal properties as they predict the ability of compounds to inhibit the formation or disrupt biofilms, which is an important mediator of fungal pathogenicity and treatment resistance.

10.2.1 Biofilm Quantification

Crystal violet (CV) staining is a powerful technique to estimate biofilm biomass. For this test, yeast cells of C. albicans are grown on microtiter plate in the presence or absence of indole derivatives. Following the incubation period, non-adherent cells are washed off and the remaining biofilm is stained with CV. The dye is subsequently solubilized and absorbance is recorded using a spectrophotometer as an indicator of biofilm biomass. For example, 7-

benzyloxyindole could reduce the formation of biofilm by as much as 94% at a concentration of 0.1 mM, and at the same concentration, with higher effect than fluconazole.[121]

10.2.3 Comparative Study and Implications for indole derivatives

Comparative analyses of CLSI and EUCAST methods have shown excellent concordance in MICs of antifungal drugs. For example, a survey of the 2 methods to test itraconazole, posaconazole, and voriconazole by use of Aspergillus species resulted in essential agreement from 98.4% to 100% within ±2 dilutions.[122]

In assessing new antifungal agents, including indole compounds, it is important to be faithful to the BMD reference methods in order to obtain reliable and comparable results. These approaches permit its antifungal potency to be evaluated and compared with that of other antifungal drugs. Also, the comparative use of both CLSI and EUCAST reference methods can give a fuller picture of a compound's activity against fungi in different testing scenarios.[123]

10.3 Assay of metabolic activity

Evaluation of metabolic activity of indole derivatives in antifungal therapy is necessary to characterize theirpharmacological profile. Metabolic differences are usually investigated by determining adenosine triphosphate (ATP) production, tetrazolium reduction or biofilm biomass, to get an idea of cellular metabolic activity of the fungi when exposed to drugs. E.g., it has been shown that the metabolic activity of *C. neoformans* biofilms can be significantly suppressed by itraconazole and amphotericin B treatment, standards antifungal agents, although it is difficult for these agents to penetrate into deeper layers of biofilms.[124]

In addition, investigations of resistant Candida species report differences in glutathione content that may result in the modulation of antifungal efficacy, such as that of fluconazole and micafungin.[6] This change in metabolism provides a framework for how mechanisms of resistance may develop in pathogenic fungi and may help in the design of anti-fungal drugs. Synergy studies with CSA and different antifungals have demonstrated that biofilms become more sensitive to treatment (resistant strains as well), it has been hypothesized that treatment with metabolic modulator would recover effectiveness of antifungal drugs.[125][126][127]

10.4 In vivo evaluation model

10.4.1 Murine models of systemic candidiasis or aspergillosis

Murine models are a powerful tool for investigating systemic infections with *Candida and Aspergillus spp*. The models enable human-stimulated infection and monitoring of the therapeutic responses of potential antifungal drugs. For example, *C. albicans*, a frequent-pathogenic species has been tackled employing a number of recent indole derivatives. Sarı and Kart described synthesis and evaluation of indole-based azole derivatives as antifungals, providing a strong evidence of adopted approach to generate new potential candidates to combat systemic candidiasis, especially at a time when we are encountering more and more drug resistance in clinical setting.[128] In addition, a new 1,2,4-triazole-indole hybrid has been reported to exhibit good in vitro activity against a number of fungal strains, including Aspergillus.[129] This would indicate that it is possible to increase antifungal activity of indole derivatives by introducing structural modifications. The pharmacological examination of indole derivatives does not only include in vitro studies, but also multiple in vivo assays by applying murine models. It is exemplified by novel indole structure modified compounds which have been screened as for their acute toxicological profile, and antifungal efficacy against established pathogens. Reading such parameters can report on efficacy and safety, important for clinical translation. Indole linked triazoles derivatives as reported by Na, have manifested remarkable antifungal activity in the presented in vivo models.[130] In addition, it is crucial to choose suitable in vivo models in these studies. In immunocompromised individuals the hematological system can potentially be systemic if left untreated in addition it is challenging to test the antifungal compounds in a biologically relevant system.[131] This means that even models that capture the host immune response (together with the host responses to pathogenic fungi), including those developed under conditions of murine coinfections, will give insight into the more general pharmacokinetic and pharmacodynamic behaviour of the indole agents. Dual-mechanism compounds, like compounds with triazole and indole motifs, could use disease-relevant targets, potentially improving therapeutic applications. The in vivo potential of these novel compounds was supported by their activities in murine models, exhibiting substantial reductions in fungal burdens and enhanced survivability indices when screened against Aspergillus by using assays including the microdilution broth method.[132]

11. CONCLUSION

The exploration of indole-derived compounds revealed the presence of several biologically active and therapeutically useful substances with antifungal properties. Indole as well as its derivatives have been the center of attention in medicinal chemistry because of the wide range of biological activities like antifungal activity. This particular synthesis seeks to provide a holistic approach to the outcome of the various studies that seek to explore the therapeutic possibilities of indole derivatives in antifungal treatment and their effectiveness against some of the most notorious fungi. Looking carefully at indole derivatives, it is possible to formulate an effective antifungal therapy to meet the challenges posed by the increasing antifungal resistance of prevalent pathogens. Countless studies have shown that indole derivatives are active against resistant fungal strains. This certainly supports the development of indole-based antifungal agents to optimize modern therapy. Continued research on various synthetic avenues of novel indole derivative development suggests that researchers are better positioned to design these compounds with specific interaction targets, selective lethal dose increase, and minimal noxious effects. In particular, the successful synthesis of indole-linked azoles suggests new potential pathways toward the development of novel antifungal agents. There is sufficient literature backing the claim that careful additional work aimed at the extensive modification of these derivatives will effectively develop potent antifungal therapies targeted for clinical use. Furthermore, a wider interest intending to clarify the action mechanism of indole-based compounds is in docking analysis along with computational chemistry. Such methods help not only in estimating the biological activity of new derivatives, but also in studying the mechanisms of resistance in infectious fungi . Therefore, knowledge of molecular interaction can better direct the design of new drugs which attempt to evade known pathways of resistance, and potentially ease the clinical problem of fungal infections. The synergistic integration of organic chemistry, pharmacology, and molecular biology has led to a deepened understanding of the unique ways in which indole derivatives exhibit antifungal activity. Of considerable relevance, the variety of structures that can be synthesized from indole offers limitless potential for the creation of therapeutic agents. More of such compounds can be developed by focusing on biological testing of new indole derivatives, along with studying the mechanisms behind their antifungal activities to increase their effectiveness for the clinical scenario. Concerns related to bioavailability and toxicity are still relevant; however, there is opportunity for innovation on the effectiveness of indole derivatives as antifungal agents with a few tweaks. In essence, dynamic developments of synthetic methodologies and further research into the chemistry of

indole could provide important advances for treating fungal infections, ensuring the continued relevance of these compounds in antimicrobial medicine.

REFERENCES

1. Z. Bai, K. Dang, J. Tang, R. Yang, L. Fan, L. Qiuet al., "Synthesis, characterization, and evaluation of the antifungal properties of 3-indolyl-3-hydroxy oxindole derivatives against plant pathogenic fungi", Molecules, 2025; 30, 5: 1079. https://doi.org/10.3390/molecules30051079.
2. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
3. V. Kumar, S. Sharma, S. Singh, A. Kumar, & S. Sharma, "Synthesis and evaluation of novel indolylthiadiazinoazetidinones and indolylthiadiazinothiazolidinones as antimicrobial agents", Archiv Der Pharmazie, 2010; 343, 2: 98-107. https://doi.org/10.1002/ardp.200900203.
4. A. Fuentefría, B. Pippi, D. Lana, K. Donato, & S. Andrade, "Antifungals discovery: an insight into new strategies to combat antifungal resistance", Letters in Applied Microbiology, 2018; 66, 1: 2-13. https://doi.org/10.1111/lam.12820.
5. S. Seyedjavadi, F. Hatami, & Z. Jahanshiri, "Antifungal resistance in candida albicans", 2024. https://doi.org/10.5772/intechopen.1004578
6. J. Kim, S. Park, G. Noh, H. Kim, S. Yoo, I. Kimet al., "Antifungal effect of a chimeric peptide hn-mc against pathogenic fungal strains", Antibiotics, 2020; 9, 8: 454. https://doi.org/10.3390/antibiotics9080454
7. P. Sakinala, M. Vemula, G. Komre, S. Kattupalli, S. Kondamudi, & L. Lagadapati, "A comprehensive knowledge on review of indole derivatives", International Journal of Pharma and Bio Sciences, 2021; 11, 4: 19-24. https://doi.org/10.22376/ijpbs/lpr.2021.11.4.p19-24
8. P. Jain, D. Utreja, & P. Sharma, "An efficacious synthesis of n-1–, c-3–substituted indole derivatives and their antimicrobial studies", Journal of Heterocyclic Chemistry, 2019; 57, 1: 428-435. https://doi.org/10.1002/jhet.3799.
9. H. Xu and L. Fan, "Antifungal agents. part 4: synthesis and antifungal activities of novel indole[1,2-c]-1,2,4-benzotriazine derivatives against phytopathogenic fungi in vitro", European Journal of Medicinal Chemistry, 2011; 46, 1: 364-369. https://doi.org/10.1016/j.ejmech.2010.10.022.

10. S. Ölgen, A. Kaeßler, D. Nebioğlu, & J. Jose, "Research letter: new potent indole derivatives as hyaluronidase inhibitors", Chemical Biology & Drug Design, 2007; 70, 6: 547-551. https://doi.org/10.1111/j.1747-0285.2007.00590.x.
11. A. Suresh, V. Meenakumari, P. kalairasi, T. Kanimozhi, & S. Ramakrishnan, "Design, synthesis and invitro biological evaluation of benzothiazole, indole and imidazole derivatives as anti tubercular agents targeting glutamine synthetase-1", 2020. https://doi.org/10.21203/rs.3.rs-52122/v1.
12. T. Banerjee, D. Kar, P. Krishna, S. Prabhakar, R. Nomula, V. Mallulaet al., "A novel triazine-aryl-bis-indole derivative inhibits both phosphodiesterase iv and expression of cell adhesion molecules", RSC Advances, 2015; 5, 86: 70271-70281. https://doi.org/10.1039/c5ra11495k.
13.] I. Kruk, H. Aboul-Enein, T. Michalska, K. Lichszteld, K. Kubasik-Kładna, & S. Ölgen, "in vitro scavenging activity for reactive oxygen species by n-substituted indole-2-carboxylic acid esters", Luminescence, 2007; 22, 4: 379-386. https://doi.org/10.1002/bio.974.
14. F. Zhao and Z. Liu, "Indole and its alkyl-substituted derivatives protect erythrocyte and dna against radical-induced oxidation", Journal of Biochemical and Molecular Toxicology, 2009; 23, 4: 273-279. https://doi.org/10.1002/jbt.20289.
15. K. Sue, M. Cadelis, E. Gill, F. Rouvier, M. Bourguet-Kondracki, J. Brunelet al., "Indole-3-acetamido-polyamines as antimicrobial agents and antibiotic adjuvants", Biomolecules, 2023; 13, 8: 1226. https://doi.org/10.3390/biom13081226.
16. Y. Na, "Synthesis and activity of novel indole linked triazole derivatives as antifungal agents", Cheminform, 2011; 42: 13. https://doi.org/10.1002/chin.201113166.
17. H. Xu, Q. Wang, & Y. Wen-bin, "Antifungal activities of some indole derivatives", Zeitschrift Für Naturforschung C, 2010; 65, 7-8: 437-439. https://doi.org/10.1515/znc-2010-7-803.
18. A. Kurmi, A. Singh, Y. Gautam, N. Singh, A. Tripathi, A. Negiet al., "Gallic acid derived 1, 2-diarylindole as a potential antifungal agent against candida strain", Current Topics in Medicinal Chemistry, 2024; 24. https://doi.org/10.2174/0115680266278892240102045630.
19. J. Strigáčová, D. Hudecová, M. Mikulášová, Ľ. Varečka, A. Lásiková, & D. Végh, "Novel oxindole derivatives and their biological activity", Folia Microbiologica, 2001; 46, 3: 187-192. https://doi.org/10.1007/bf02818531.

20. P. Sakinala, K. Rahaman, V. Mounika, & K. Sathvika, "A comprehensive knowledge on review of indole derivatives", International Journal of Life Science and Pharma Research, 2021. https://doi.org/10.22376/ijpbs/lpr.2021.11.4.p19-p24.
21. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies", Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.
22. H. Xu and T. Li, "Recent progress of bioactivities, mechanisms of action, total synthesis, structural modifications and structure-activity relationships of indole derivatives: a review", Mini-Reviews in Medicinal Chemistry, 2022; 22, 21: 2702-2725. https://doi.org/10.2174/1389557522666220330123538.
23. D. Zampieri, M. Mamolo, E. Laurini, G. Scialino, E. Banfi, & L. Vio, "2-aryl-3-(1h-azol-1-yl)-1h-indole derivatives: a new class of antimycobacterial compounds – conventional heating in comparison with mw-assisted synthesis", Archiv Der Pharmazie, 2009; 342, 12: 716-722. https://doi.org/10.1002/ardp.200900031.
24. T. Sasaki, Y. Igarashi, M. Ogawa, & T. FURUMAI, "Identification of 6-prenylindole as an antifungal metabolite of streptomyces sp. tp-a0595 and synthesis and bioactivity of 6-substituted indoles.", Cheminform, 2003; 34: 19. https://doi.org/10.1002/chin.200319203\.
25. P. Kutschy, M. Suchý, M. Dzurilla, M. Takasugi, & V. Kováčik, "A new approach to imidazo[1,5-a] indole derivatives", Collection of Czechoslovak Chemical Communications, 2000; 65, 7: 1163-1172. https://doi.org/10.1135/cccc20001163.
26. P. Kumar, P. Bora, A. Kumar, A. Singh, H. Singh, & B. Narasimhan, "Molecular docking and qsar studies of indole derivatives as antifungal agents", Current Chinese Chemistry, 2023; 3. https://doi.org/10.2174/2666001603666230328181833.
27. M. Sofan, F. El-Ablack, & A. Elsayed, "Antimicrobial activity of n-substituted derivatives of 5-chloro-2,3- diphenyl indole", Chemistryselect, 2023; 8: 46. https://doi.org/10.1002/slct.202302922.
28. S. Ölgen, N. Altanlar, E. Karataylı, & M. Bozdayı, "Antimicrobial and antiviral screening of novel indole carboxamide and propanamide derivatives", Zeitschrift Für Naturforschung C, 2008; 63, 3-4: 189-195. https://doi.org/10.1515/znc-2008-3-405.

29. H. Cai, R. Li, Y. Chen, R. Bi, X. Fang, P. Wuet al., "Rational modification of melatonin for broad-spectrum antifungal agents discovery", Journal of Pineal Research, 2024; 76: 4. https://doi.org/10.1111/jpi.12960.
30. S. Zheng, Q. Jiang, G. Massande, W. Wen-bin, C. Lin, Y. Fanget al., "Synthesis and antifungal activity of indole derivatives", Chemistry of Natural Compounds, 2023; 59, 1: 111-118. https://doi.org/10.1007/s10600-023-03929-5.
31. M. Wang, Z. Qu, D. Du, & L. Jiang, "Synthesis and antifungal activity of novel 1-(3-indoly)-3-aryl-2-propen-1-one oxime ethers", Chinese Journal of Organic Chemistry, 2013; 33, 5: 1005. https://doi.org/10.6023/cjoc201212025.
32. I. Mushtaq and A. Ahmed, "Synthesis of biologically active sulfonamide-based indole analogs: a review", Future Journal of Pharmaceutical Sciences, 2023; 9: 1. https://doi.org/10.1186/s43094-023-00500-5.
33. M. Rani, D. Utreja, & S. Sharma, "Role of indole derivatives in agrochemistry: synthesis and future insights", Current Organic Chemistry, 2022; 26, 7: 651-678. https://doi.org/10.2174/1385272826666220426103835.
34. S. Beula, T. Reddy, R. Suthakaran, & K. Suneetha, "A review on isatin, isatin derivatives and their pharmacological activity", Research Journal of Pharmacology and Pharmacodynamics, 2021; 59-62. https://doi.org/10.52711/2321-5836.2021.00013.
35. T. Li, M. Lv, H. Wen, J. Du, Z. Wang, S. Zhanget al., "Natural products in crop protection: thiosemicarbazone derivatives of 3-acetyl-n-benzylindoles as antifungal agents and their mechanism of action", Pest Management Science, 2023; 79, 8: 2801-2810. https://doi.org/10.1002/ps.7457.
36. H. Xu, Q. Wang, & Y. Wen-bin, "Antifungal activities of some indole derivatives", Zeitschrift Für Naturforschung C, 2010; 65, 7-8: 437-439. https://doi.org/10.1515/znc-2010-7-803.
37. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
38. I. Singh, "Synthesis and evaluation of some newly triazolylindole derivatives for antifungal activity", International Research Journal of Pharmacy, 2014; 5, 12: 891-895. https://doi.org/10.7897/2230-8407.0512181.
39. I. Jerković, S. Prđun, Z. Marijanović, M. Zekić, D. Bubalo, L. Svečnjaket al., "Traceability of satsuma mandarin (citrus unshiu marc.) honey through nectar/honey-

sac/honey pathways of the headspace, volatiles, and semi-volatiles: chemical markers", Molecules, 2016; 21, 10: 1302. https://doi.org/10.3390/molecules21101302.

40. B. Bertinetti, M. Scandiani, & G. Cabrera, "Analogs of antifungal indoles isolated from aporpium caryae with activity against sudden-death syndrome of soybean", American Journal of Plant Sciences, 2011; 02, 02: 245-254. https://doi.org/10.4236/ajps.2011.22026.
41. J. Bao, C. Xu, G. Yang, C. Wang, X. Zheng, & X. Yuan, "Novel 6a,12b-dihydro-6h,7h-chromeno[3,4-c] chromen-6-ones: synthesis, structure and antifungal activity", Molecules, 2019; 24, 9: 1745. https://doi.org/10.3390/molecules24091745.
42. D. Huang, Z. He, D. Guo, F. Deng, Q. Bian, H. Zhanget al., "Discovery of novel benzoxaborole-containing streptochlorin derivatives as potential antifungal agents", Journal of Agricultural and Food Chemistry, 2023; 71, 16: 6226-6235. https://doi.org/10.1021/acs.jafc.2c08053.
43. J. Kaur, D. Utreja, N. Jain, & S. Sharma, "Recent developments in the synthesis and antimicrobial activity of indole and its derivatives", Current Organic Synthesis, 2019; 16, 1: 17-37. https://doi.org/10.2174/1570179415666181113144939.
44. D. Singh, R. Kharb, S. Sharma, & V. Kumar, "Phytochemical and pharmacological intervention of indole and their derivatives: a comprehensive review", Natural Resources for Human Health, 2024; 4, 3: 308-317. https://doi.org/10.53365/nrfhh/188891.
45. R. Li, R. Bi, H. Cai, J. Zhao, P. Sun, W. Xuet al., "Melatonin functions as a broad-spectrum antifungal by targeting a conserved pathogen protein kinase", Journal of Pineal Research, 2022; 74: 1. https://doi.org/10.1111/jpi.12839.
46. Y. Na, "Synthesis and activity of novel indole linked triazole derivatives as antifungal agents", Bulletin of the Korean Chemical Society, 2010; 31, 11: 3467-3470. https://doi.org/10.5012/bkcs.2010.31.11.3467.
47. J. Liu, Y. Gao, B. Jin, D. Guo, F. Deng, Q. Bianet al., "Design, synthesis, antifungal activity, and molecular docking of streptochlorin derivatives containing the nitrile group", Marine Drugs, 2023; 21, 2: 103. https://doi.org/10.3390/md21020103.
48. B. Pippi, W. Lopes, P. Reginatto, F. Silva, A. Joaquim, R. Alveset al., "New insights into the mechanism of antifungal action of 8-hydroxyquinolines", Saudi Pharmaceutical Journal, 2019; 27: 1: 41-48. https://doi.org/10.1016/j.jsps.2018.07.017.
49. J. Bao, C. Xu, G. Yang, C. Wang, X. Zheng, & X. Yuan, "Novel 6a,12b-dihydro-6h,7h-chromeno[3,4-c] chromen-6-ones: synthesis, structure and antifungal activity", Molecules, 2019; 24, 9: 1745. https://doi.org/10.3390/molecules24091745.

50. H. Xu, Q. Wang, & Y. Wen-bin, "Antifungal activities of some indole derivatives", Zeitschrift Für Naturforschung C, 2010; 65, 7-8: 437-439. https://doi.org/10.1515/znc-2010-7-803.
51. M. Rani, D. Utreja, & S. Sharma, "Role of indole derivatives in agrochemistry: synthesis and future insights", Current Organic Chemistry, 2022; 26, 7: 651-678. https://doi.org/10.2174/1385272826666220426103835.
52. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
53. I. Singh, "Synthesis and evaluation of some newly triazolylindole derivatives for antifungal activity", International Research Journal of Pharmacy, 2014; 5, 12: 891-895. https://doi.org/10.7897/2230-8407.0512181.
54. J. Kim, S. Park, G. Noh, H. Kim, S. Yoo, I. Kimet al., "Antifungal effect of a chimeric peptide hn-mc against pathogenic fungal strains", Antibiotics, 2020; 9, 8: 454. https://doi.org/10.3390/antibiotics9080454.
55. F. Zhao and Z. Liu, "Indole and its alkyl-substituted derivatives protect erythrocyte and dna against radical-induced oxidation", Journal of Biochemical and Molecular Toxicology, 2009; 23, 4: 273-279. https://doi.org/10.1002/jbt.20289.
56. P. Jain, D. Utreja, & P. Sharma, "An efficacious synthesis of n-1–, c-3–substituted indole derivatives and their antimicrobial studies", Journal of Heterocyclic Chemistry, 2019; 57, 1: 428-435. https://doi.org/10.1002/jhet.3799.
57. A. Fuentefría, B. Pippi, D. Lana, K. Donato, & S. Andrade, "Antifungals discovery: an insight into new strategies to combat antifungal resistance", Letters in Applied Microbiology, 2018; 66, 1: 2-13. https://doi.org/10.1111/lam.12820.
58. A. Kurmi, A. Singh, Y. Gautam, N. Singh, A. Tripathi, A. Negiet al., "Gallic acid derived 1, 2-diarylindole as a potential antifungal agent against candida strain", Current Topics in MedicinalChemistry, 2024; 24. https://doi.org/10.2174/0115680266278892240102045630.
59. M. Sofan, F. El-Ablack, & A. Elsayed, "Antimicrobial activity of n-substituted derivatives of 5-chloro-2,3- diphenyl indole", Chemistryselect, 2023; 8: 46. https://doi.org/10.1002/slct.202302922.
60. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies",

Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.

61. T. Banerjee, D. Kar, P. Krishna, S. Prabhakar, R. Nomula, V. Mallula et al., "A novel triazine-aryl-bis-indole derivative inhibits both phosphodiesterase iv and expression of cell adhesion molecules", RSC Advances, 2015; 5, 86: 70271-70281. https://doi.org/10.1039/c5ra11495k.
62. S. Ölgen, A. Kaeßler, D. Nebioğlu, & J. Jose, "Research letter: new potent indole derivatives as hyaluronidase inhibitors", Chemical Biology & Drug Design, 2007; 70, 6: 547-551. https://doi.org/10.1111/j.1747-0285.2007.00590.x.
63. H. Xu and L. Fan, "Antifungal agents. Part 4: synthesis and antifungal activities of novel indole[1,2-c]-1,2,4-benzotriazine derivatives against phytopathogenic fungi in vitro", European Journal of Medicinal Chemistry, 2011; 46, 1: 364-369. https://doi.org/10.1016/j.ejmech.2010.10.022.
64. P. Sakinala, M. Vemula, G. Komre, S. Kattupalli, S. Kondamudi, & L. Lagadapati, "A comprehensive knowledge on review of indole derivatives", International Journal of Pharma and Bio Sciences, 2021; 11, 4: 19-24. https://doi.org/10.22376/ijpbs/lpr.2021.11.4.p19-24.
65. A. Suresh, V. Meenakumari, P. Kalairasi, T. Kanimozhi, & S. Ramakrishnan, "Design, synthesis, and invitro biological evaluation of benzothiazole, indole, and imidazole derivatives as anti-tubercular agents targeting glutamine synthetase-1", 2020. https://doi.org/10.21203/rs.3.rs-52122/v1.
66. S. Seyedjavadi, F. Hatami, & Z. Jahanshiri, "Antifungal resistance in candida albicans", 2024. https://doi.org/10.5772/intechopen.1004578.
67. J. Kim, S. Park, G. Noh, H. Kim, S. Yoo, I. Kim et al., "Antifungal effect of a chimeric peptide hn-mc against pathogenic fungal strains", Antibiotics, 2020; 9, 8: 454. https://doi.org/10.3390/antibiotics9080454.
68. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies", Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.
69. P. Jain, D. Utreja, & P. Sharma, "An efficacious synthesis of n-1–, c-3–substituted indole derivatives and their antimicrobial studies", Journal of Heterocyclic Chemistry, 2019; 57, 1: 428-435. https://doi.org/10.1002/jhet.3799.

70. T. Banerjee, D. Kar, P. Krishna, S. Prabhakar, R. Nomula, V. Mallula et al., "A novel triazine-aryl-bis-indole derivative inhibits both phosphodiesterase iv and expression of cell adhesion molecules", RSC Advances, 2015; 5, 86: 70271-70281. https://doi.org/10.1039/c5ra11495k.
71. M. Rani, D. Utreja, & S. Sharma, "Role of indole derivatives in agrochemistry: synthesis and future insights", Current Organic Chemistry, 2022; 26, 7: 651-678. https://doi.org/10.2174/1385272826666220426103835.
72. H. Cai, R. Li, Y. Chen, R. Bi, X. Fang, P. Wu et al., "Rational modification of melatonin for broad-spectrum antifungal agents discovery", Journal of Pineal Research, 2024; 76: 4. https://doi.org/10.1111/jpi.12960.
73. F. Zhao and Z. Liu, "Indole and its alkyl-substituted derivatives protect erythrocyte and dna against radical-induced oxidation", Journal of Biochemical and Molecular Toxicology, 2009; 23, 4: 273-279. https://doi.org/10.1002/jbt.20289.
74. I. Mushtaq and A. Ahmed, "Synthesis of biologically active sulfonamide-based indole analogs: a review", Future Journal of Pharmaceutical Sciences, 2023; 9: 1. https://doi.org/10.1186/s43094-023-00500-5.
75. S. Ölgen, A. Kaeßler, D. Nebioğlu, & J. Jose, "Research letter: new potent indole derivatives as hyaluronidase inhibitors", Chemical Biology & Drug Design, 2007; 70, 6: 547-551. https://doi.org/10.1111/j.1747-0285.2007.00590.x.
76. J. Liu, Y. Gao, B. Jin, D. Guo, F. Deng, Q. Bian et al., "Design, synthesis, antifungal activity, and molecular docking of streptochlorin derivatives containing the nitrile group", Marine Drugs, 2023; 21, 2: 103. https://doi.org/10.3390/md21020103.
77. J. Bao, C. Xu, G. Yang, C. Wang, X. Zheng, & X. Yuan, "Novel 6a,12b-dihydro-6h,7h-chromeno[3,4-c] chromen-6-ones: synthesis, structure and antifungal activity", Molecules, 2019; 24, 9: 1745. https://doi.org/10.3390/molecules24091745.
78. Y. Zhao, M. Su, J. Shang, X. Wang, G. Njateng, G. Bao et al., "Acute and chronic toxicity of indole alkaloids from leaves of alstonia scholaris (l.) r. br. in mice and rats", Natural Products and Bioprospecting, 2020; 10, 2: 77-88. https://doi.org/10.1007/s13659-020-00237-1.
79. P. Sakinala, K. Rahaman, V. Mounika, & K. Sathvika, "A comprehensive knowledge on review of indole derivatives", International Journal of Life Science and Pharma Research, 2021. https://doi.org/10.22376/ijpbs/lpr.2021.11.4.p19-p24.
80. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies",

Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.

81. H. Xu and L. Fan, "Antifungal agents. Part 4: synthesis and antifungal activities of novel indole[1,2-c]-1,2,4-benzotriazine derivatives against phytopathogenic fungi in vitro", European Journal of Medicinal Chemistry, 2011; 46, 1, 364-369. https://doi.org/10.1016/j.ejmech.2010.10.022.
82. M. Wang, Z. Qu, D. Du, & L. Jiang, "Synthesis and antifungal activity of novel 1-(3-indoly)-3-aryl-2-propen-1-one oxime ethers", Chinese Journal of Organic Chemistry, 2013; 33, 5: 1005. https://doi.org/10.6023/cjoc201212025.
83. A. Kurmi, A. Singh, Y. Gautam, N. Singh, A. Tripathi, A. Negiet al., "Gallic acid derived 1, 2-diarylindole as a potential antifungal agent against candida strain", Current Topics in Medicinal Chemistry, 2024; 24. https://doi.org/10.2174/0115680266278892240102045630.
84. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies", Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.
85. S. Beula, T. Reddy, R. Suthakaran, & K. Suneetha, "A review on isatin, isatin derivatives and their pharmacological activity", Research Journal of Pharmacology and Pharmacodynamics, 2021; 59-62. https://doi.org/10.52711/2321-5836.2021.00013.
86. M. Sofan, F. El-Ablack, & A. Elsayed, "Antimicrobial activity of n-substituted derivatives of 5-chloro-2,3-diphenyl indole", Chemistryselect, 2023; 8: 46. https://doi.org/10.1002/slct.202302922.
87. T. Banerjee, D. Kar, P. Krishna, S. Prabhakar, R. Nomula, V. Mallula et al., "A novel triazine-aryl-bis-indole derivative inhibits both phosphodiesterase iv and expression of cell adhesion molecules", RSC Advances, 2015; 5, 86: 70271-70281. https://doi.org/10.1039/c5ra11495k.
88. H. Xu and T. Li, "Recent progress of bioactivities, mechanisms of action, total synthesis, structural modifications, and structure-activity relationships of indole derivatives: a review", Mini-Reviews in Medicinal Chemistry, 2022; 22, 21: 2702-2725. https://doi.org/10.2174/1389557522666220330123538.
89. S. Ölgen, N. Altanlar, E. Karataylı, & M. Bozdayı, "Antimicrobial and antiviral screening of novel indole carboxamide and propanamide derivatives", Zeitschrift Für Naturforschung C, 2008; 63, 3-4: 189-195. https://doi.org/10.1515/znc-2008-3-405.

90. Y. Zhao, M. Su, J. Shang, X. Wang, G. Njateng, G. Bao et al., "Acute and chronic toxicity of indole alkaloids from leaves of alstonia scholaris (l.) r. br. in mice and rats", Natural Products and Bioprospecting, 2020; 10, 2: 77-88. https://doi.org/10.1007/s13659-020-00237-.
91. H. Shirinzadeh, S. Süzen, N. Altanlar, & A. Westwell, "Antimicrobial activities of new indole derivatives containing 1,2,4-triazole, 1,3,4-thiadiazole and carbothioamide", Turkish Journal of Pharmaceutical Sciences, 2018. https://doi.org/10.4274/tjps.55707.
92. Z. Bai, K. Dang, J. Tang, R. Yang, L. Fan, L. Qiuet al., "Synthesis, characterization, and evaluation of the antifungal properties of 3-indolyl-3-hydroxy oxindole derivatives against plant pathogenic fungi", Molecules, 2025; 30, 5: 1079. https://doi.org/10.3390/molecules30051079.
93. B. He, Y. Hu, X. Li, Y. Qing, K. Meng, W. Zenget al., "Antifungal activity of novel indole derivatives containing 1,3,4-thiadiazole", Journal of Agricultural and Food Chemistry, 2024; 72, 18: 10227-10235. https://doi.org/10.1021/acs.jafc.3c09303.
94. R. Rather and T. Ara, "Synthesis, biological evaluation and docking studies of 4h-[1,2,3] thiadiazolo[4,5-b]indole hybrids as antifungal agents", Chemistryselect, 2023; 8: 14. https://doi.org/10.1002/slct.202202978.
95. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
96. F. Pagniez, N. Lebouvier, Y. Na, I. Ourliac-Garnier, C. Picot, M. Borgneet al., "Biological exploration of a novel 1,2,4-triazole-indole hybrid molecule as antifungal agent", Journal of Enzyme Inhibition and Medicinal Chemistry, 2020; 35, 1: 398-403. https://doi.org/10.1080/14756366.2019.1705292.
97. N. Lebouvier, F. Pagniez, Y. Na, D. Shi, P. Recordon-Pinson, M. Marchivieet al., "Synthesis, optimization, antifungal activity, selectivity, and cyp51 binding of new 2-aryl-3-azolyl-1-indolyl-propan-2-ols", Pharmaceuticals, 2020; 13 8: 186. https://doi.org/10.3390/ph13080186.
98. T. Li, M. Lv, H. Wen, J. Du, Z. Wang, S. Zhanget al., "Natural products in crop protection: thiosemicarbazone derivatives of 3-acetyl-n-benzylindoles as antifungal agents and their mechanism of action", Pest Management Science, 2023; 79, 8: 2801-2810. https://doi.org/10.1002/ps.7457.

99. A. Kumar, D. Kumari, H. Singh, A. Mishra, & A. Mishra, "Recent advancements in indole derivatives and their antimicrobial perspective", Letters in Organic Chemistry, 2023; 20, 8: 730-754. https://doi.org/10.2174/1570178620666230306092300.
100. X. Mo, D. Rao, K. Kaur, R. Hassan, A. Abdel-Samea, S. Farhanet al., "Indole derivatives: a versatile scaffold in modern drug discovery—an updated review on their multifaceted therapeutic applications (2020–2024)", Molecules, 2024; 29, 19: 4770. https://doi.org/10.3390/molecules29194770.
101. M. Wang, Z. Qu, D. Du, & L. Jiang, "Synthesis and antifungal activity of novel 1-(3-indoly)-3-aryl-2-propen-1-one oxime ethers", Chinese Journal of Organic Chemistry, 2013; 33, 5: 1005. https://doi.org/10.6023/cjoc201212025.
102.] A. Kurmi, A. Singh, Y. Gautam, N. Singh, A. Tripathi, A. Negiet al., "Gallic acid derived 1, 2-diarylindole as a potential antifungal agent against candida strain", Current Topics in Medicinal Chemistry, 2024; 24. https://doi.org/10.2174/0115680266278892240102045630.
103. D. Kumar, S. Sharma, S. Kalra, G. Singh, V. Monga, & B. Kumar, "Medicinal perspective of indole derivatives: recent developments and structure-activity relationship studies", Current Drug Targets, 2020; 21, 9: 864-891. https://doi.org/10.2174/1389450121666200310115327.
104. P. Kumar, P. Bora, A. Kumar, A. Singh, H. Singh, & B. Narasimhan, "Molecular docking and qsar studies of indole derivatives as antifungal agents", Current Chinese Chemistry, 2023; 3. https://doi.org/10.2174/2666001603666230328181833.
105. N. Berdzik, B. Jasiewicz, K. Ostrowski, A. Sierakowska, M. Szlażys, D. Nowaket al., "Novel gramine-based bioconjugates obtained by click chemistry as cytoprotective compounds and potent antibacterial and antifungal agents", Natural Product Research, 2023; 38, 21: 3721-3727. https://doi.org/10.1080/14786419.2023.2261139.
106. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
107. S. Shrestha, M. Fosso, & S. Garneau-Tsodikova, "A combination approach to treating fungal infections", Scientific Reports, 2015; 5: 1. https://doi.org/10.1038/srep17070.
108. A. Ahmad, M. Wani, M. Patel, A. Sobral, A. Dusé, F. Aqlanet al., "Synergistic antifungal effect of cyclized chalcone derivatives and fluconazole against candida albicans", Medchemcomm, 2017; 8, 12: 2195-2207. https://doi.org/10.1039/c7md00440k.

109. V. Sharma, G. Brahmachari, & V. Gupta, "Crystallographic structure, activity prediction, and hydrogen bonding analysis of some csd-based 3,3'-bis-indole derivatives: a review", European Journal of Chemistry, 2021; 12, 4: 493-501. https://doi.org/10.5155/eurjchem.12.4.493-501.2145.
110. Y. Na, "Synthesis and activity of novel indole linked triazole derivatives as antifungal agents", Bulletin of the Korean Chemical Society, 2010; 31, 11: 3467-3470. https://doi.org/10.5012/bkcs.2010.31.11.3467.
111. S. El-Sayed, N. Abdelaziz, A. Ali, M. Alshahrani, K. Aboshanab, & G. El-Housseiny, "Identification, characterization, and production optimization of 6-methoxy-1h-indole-2-carboxylic acid antifungal metabolite produced by bacillus toyonensis isolate oq071612", Microorganisms, 2023; 11, 12: 2835. https://doi.org/10.3390/microorganisms11122835.
112. X. Han, Y. Zhong, S. Li, G. Liang, G. Zhou, X. Wanget al., "Synthesis, characterization and antifungal evaluation of novel thiochromanone derivatives containing indole skeleton", Chemical and Pharmaceutical Bulletin, 2016; 64, 9: 1411-1416. https://doi.org/10.1248/cpb.c16-00366.
113. S. Sarı, D. Kart, S. Sabuncuoğlu, İ. Doğan, Z. Özdemir, İ. Bozbeyet al., "Antifungal screening and in silico mechanistic studies of an in-house azole library", Chemical Biology & Drug Design, 2019; 94, 5: 1944-1955. https://doi.org/10.1111/cbdd.13587
114. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
115. C. Wang, H. Song, W. Liu, & C. Xu, "Design, synthesis and antifungal activity of novel thioureas containing 1,3,4-thiadiazole and thioether skeleton", Chemical Research in Chinese Universities, 2016; 32, 4: 615-620. https://doi.org/10.1007/s40242-016-6023-8
116. Z. Bai, K. Dang, J. Tang, R. Yang, L. Fan, L. Qiuet al., "Synthesis, characterization, and evaluation of the antifungal properties of 3-indolyl-3-hydroxy oxindole derivatives against plant pathogenic fungi", Molecules, 2025; 30, 5: 1079. https://doi.org/10.3390/molecules30051079.
117. M. Sofan, F. El-Ablack, & A. Elsayed, "Antimicrobial activity of n-substituted derivatives of 5-chloro-2,3- diphenyl indole", Chemistryselect, 2023; 8: 46. https://doi.org/10.1002/slct.202302922.

118. R. Al-Wabli, M. Alsulami, S. Bukhari, N. Moubayed, M. Almutairi, & M. Attia, "Design, synthesis, and antimicrobial activity of certain new indole-1,2,4 triazole conjugates", Molecules, 2021; 26, 8: 2292. https://doi.org/10.3390/molecules26082292.
119. X. Li, Y. Zhi, X. Duan, C. Xu, M. Cui, & S. Zheng, "Synergistic antifungal effects and mechanisms of amantadine hydrochloride combined with azole antifungal drugs on drug-resistant candida albicans", Frontiers in Cellular and Infection Microbiology, 2025; 15. https://doi.org/10.3389/fcimb.2025.1455123.
120. H. Xu, Q. Wang, & Y. Wen-bin, "Antifungal activities of some indole derivatives", Zeitschrift Für Naturforschung C, 2010; 65, 7-8: 437-439. https://doi.org/10.1515/znc-2010-7-803.
121. C. Orasch, O. Marchetti, J. Garbino, J. Schrenzel, S. Zimmerli, K. Mühlethaleret al., "Candida species distribution and antifungal susceptibility testing according to european committee on antimicrobial susceptibility testing and new vs. old clinical and laboratory standards institute clinical breakpoints: a 6-year prospective candidaemia survey from the fungal infection network of switzerland", Clinical Microbiology and Infection, 2014; 20, 7: 698-705. https://doi.org/10.1111/1469-0691.12440.
122. A. Espinel-Ingroff, M. Pfaller, R. Cantón, & J. Pemán, "Emerging resistance to azoles and echinocandins: clinical relevance and laboratory detection", Current Fungal Infection Reports, 2010; 4, 3: 186-195. https://doi.org/10.1007/s12281-010-0026-6.
123. M. Pfaller, G. Moet, S. Messer, R. Jones, & M. Castanheira, "candida bloodstream infections: comparison of species distributions and antifungal resistance patterns in community-onset and nosocomial isolates in the sentry antimicrobial surveillance program, 2008-2009", Antimicrobial Agents and Chemotherapy, 2011; 55, 2: 561-566. https://doi.org/10.1128/aac.01079-10.
124. M. Pfaller, D. Diekema, D. Gibbs, V. Newell, D. Ellis, V. Tullioet al., "Results from the artemis disk global antifungal surveillance study, 1997 to 2007: a 10.5-year analysis of susceptibilities of candida species to fluconazole and voriconazole as determined by clsi standardized disk diffusion", Journal of Clinical Microbiology, 2010; 48, 4: 1366-1377. https://doi.org/10.1128/jcm.02117-09.
125. F. Malayeri, A. Rezaei, & O. Raiesi, "Antifungal agents: polyene, azole, antimetabolite, other and future agents", Journal of Basic Research in Medical Sciences, 2018; 5, 2: 48-55. https://doi.org/10.29252/jbrms.5.2.48.

126. R. K. Manoharan, J. Lee, and J. Lee, “Efficacy of 7-benzyloxyindole and other halogenated indoles to inhibit Candida albicans biofilm and hyphal formation,” Microbial Biotechnology, 2018; 11, 6: 1060–1069. doi: 10.1111/1751-7915.13268.
127. J. Nett, H. Sánchez, M. Cain, & D. Andes, "Genetic basis ofcandidabiofilm resistance due to drug-sequestering matrix glucan", The Journal of Infectious Diseases, 2010; 202, 1: 171-175. https://doi.org/10.1086/651200.
128. C. Kowalski, K. Morelli, D. Schultz, C. Nadell, & R. Cramer, "Fungal biofilm architecture produces hypoxic microenvironments that drive antifungal resistance", Proceedings of the National Academy of Sciences, 2020; 117, 36: 22473-22483,. https://doi.org/10.1073/pnas.2003700117.
129. G. Araújo, R. Brilhante, M. Rocha, L. Aguiar, D. Castelo-Branco, G. Guedeset al., "Anthraquinones against cryptococcus neoformans sensu stricto: antifungal interaction, biofilm inhibition and pathogenicity in the caenorhabditis elegans model", Journal of Medical Microbiology, 2024; 73: 3. https://doi.org/10.1099/jmm.0.001815.
130. M. Mariné, V. Bom, P. Castro, L. Winkelströter, L. Ramalho, N. Brownet al., "The development of animal infection models and antifungal efficacy assays against clinical isolates oftrichosporon asahii,t. asteroidesandt. inkin", Virulence, 2015; 6, 5: 476-486. https://doi.org/10.1080/21505594.2015.1020273.
131. S. Sarı and D. Kart, "Design, synthesis, antifungal activity, and qm/mm docking study of two azole derivatives with indole ring", Journal of Research in Pharmacy, 2020; 24, 5: 681-692. https://doi.org/10.35333/jrp.2020.223.
132. F. Pagniez, N. Lebouvier, Y. Na, I. Ourliac-Garnier, C. Picot, M. Borgneet al., "Biological exploration of a novel 1,2,4-triazole-indole hybrid molecule as antifungal agent", Journal of Enzyme Inhibition and Medicinal Chemistry, 2020; 35, 1: 398-403. https://doi.org/10.1080/14756366.2019.1705292.