Click to verify



```
Triazole is a class of antifungal drugs that consists of five-membered rings with three nitrogen substitution molecules. These molecules interfere with the activity of fungal organic compounds that cause infections. Diseases TreatedFirst-generation triazoles, such as itraconazole and fluconazole, provide broad-spectrum action against superficial and
deep fungal infections. Extra nitrogens present on the triazole antifungal drugs result in increased specificity and potency compared with the older imidazole antifungals, such as miconazole. Candidiasis infections, which cause oral thrush and vaginal yeast infections, and onychomycosis, a fungal nail infection, are two common examples of diseases
treated with triazole antifungal agents. Aspergillosis, blastomycosis, histoplasmosis, and, in particular, cryptococcus meningitis, which are also treated with triazole antifungals, are more often observed in immune-compromised persons, such as those with human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome
(AIDS). Fluconazole may be used lifelong in persons with AIDS because of the increased risk of candidiasis relapse; however, prophylaxis for initial candidiasis in persons with HIV is not recommended. Mechanism of ActionTriazole antifungals disrupt sterols in fungal cytoplasmic membranes that are essential to fungal cell functioning. These drugs
bind to cytochrome P450 (CYP450) liver metabolism enzymes in the body to increase the amount of C14-alpha-methylsterol and decrease the amount of ergosterol needed by the fungal cells. Triazole effects appear proportional to drug exposure as measured by the area under the curve, and they are often longer with triazoles than with older
imidazole compounds. Triazoles, when used topically, may provide, in addition to their sterol effects and InteractionsThe most common side effects of drugs in the triazole class, when taken by mouth, are gastric discomfort, such as nausea and vomiting, and hepatotoxicity. Suppression of
the bodys sterol and hormonal levels may occur as well. The interaction of the CYP liver-enzyme system with triazole antifungals. All CYP3A4 enzymes are affected by triazole antifungals to cause inhibition of other drug of the drug of the cause increases in other drug of the cyps are taken concomitantly with triazole antifungals.
metabolism. Fluconazole and voriconazole, additionally, interact with CYP2C9 and CYP2C19 enzymes in the same manner. Drugs that are adversely increased by inhibited CYP metabolism include rifampin, midazolam, warfarin, and phenytoin; however, CYP drug interactions are specific to each triazole antifungal. ImpactFrom their early
development, which resulted from natural discovery in the 1940s, through the development of second- and third-generation agents in the early twenty-first century, triazole antifungals have expanded as a class. They now include improved action in the body and widespread administration forms, from oral to topical and nonprescription to
prescription. From the early use of itraconazole, however, resistant fungi, especially candidiasis, have developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and increased C14-alpha-demethylase changes; this resistance has led to research and developed because of drug efflux and developed because of drug ef
active against molds and zygomycetes in addition to typical fungal targets. Other late-generation examples, such as isavuconazole, ravuconazole, provide longer half-lives and improved body distribution, which improves dosing regimens also. Bibliography Greer, Nickie D. Posaconazole, ravuconazole, ravuconazole
Antifungal Agent. Proceedings (Baylor University Medical Center) 20, no. 2 (2007): 188-196. Also available at . Accessed 4 Feb. 2025. Griffith, R. K. Antifungal Drugs. In Foyes Principles of Medicinal Chemistry, edited by Thomas L. Lemke and William O. Foye. 6th ed. Philadelphia: Wolters Kluwer, 2008.Rex, John H., and David A. Stevens. Systemic
Antifungal Agents. In Mandell, Douglas, and Bennetts Principles and Practice of Infectious Diseases, edited by Gerald L. Mandell, John F. Bennett, and Raphael Dolin. 7th ed. New York: Churchill Livingstone/Elsevier, 2010.McCreary, Erin K. et al. "Utility of Triazole Antifungal Therapeutic Drug Monitoring: Insights from the Society of Infectious
Diseases Pharmacists." Pharmacotherapy, 17 July 2023, doi.org/10.1002/phar.2850. Accessed 4 Feb. 2025. Ryan, Kenneth J. Ryan and C. George Ray. 5th ed. New York: McGraw-Hill, 2010. Torres, Harry A., et al. Posaconazole: A Broad-Spectrum Triazole
Antifungal. Lancet Infectious Disease 5 (2005): 775-785. As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice . 2022 Mar 22;2022:4584846. doi:
10.1155/2022/4584846The development of innovative antifungal agents are no longer effects, and high toxicity. Therefore, the synthesis and development of some new antifungal agents are necessary. 1,2,4-Triazole is one of the most essential pharmacophore
systems between five-membered heterocycles. The structure-activity relationship (SAR) of this nitrogen-containing heterocycles compound showed potential antifungal activity of triazoles have confirmed them as
pharmacologically significant moieties. The goal of this review is to highlight recent developments in the synthesis and SAR study of 1,2,4-triazole as a potential fungicidal compound. In this study, we provide the results of a biological activity evaluation using various structures and figures. Literature investigation showed that 1, 2, 4-triazole
derivatives reveal the extensive span of antifungal activity. This review will assist researchers in the development of new potential antifungal drug candidates with high effectiveness and selectivity. Heterocyclic organic chemistry is a main field in organic and medicinal chemistry [14]. Azoles are nitrogen-containing five-membered heterocyclic
compounds [5, 6]. The presence of nitrogen in heterocycles has a major effect on biological activity. Recently, azole compounds have become hot topics around the world [2, 7]. Among the azoles fused as heterocyclic compounds have become hot topics around the world [2, 7]. Among the azoles fused as heterocycles have become hot topics around the world [2, 7].
broad ranges of biological activities, such as antimalarial [9], antiviral [11], anticonvulsant [12], antiviral [12], antiviral [13], and antifungal agents, including cyproconazole, triadimefon, metconazole, tebuconazole, propiconazole, epoxiconazole, epoxiconazole,
and prothioconazole [15]. Annually, invasive fungal infections cause 1.7 million deaths in the world, which is a major public health issue [16]. One of the most serious issues is the rise of synthetic drug resistance to various fungal pathogens; thus, the synthesis and development of new 1,2,4-triazoles with low toxicity are essential worldwide [17]. This
group of bioactive compounds acts by inhibiting the activity of cytochrome P450-dependent enzyme, the lanosterol biosynthesis [18]. Azoles link to the iron in porphyrins, causing a blockade of the fungal ergosterol biosynthesis pathway resulting in the agglomeration of 14-
demethylated sterols [19]. Recently, novel derivatives of 1,2,4-triazoles were prepared and evaluated for fungicidal activity and some of them showed potential activity against certain fungi. In previous years, many research articles have emphasized the importance of 1,2,4-triazoles as potent antifungal and antibacterial properties [2031]. However,
this review is focused on the latest papers (20152021) in the synthesis of new 1,2,4-triazole as an antifungal agent and evaluating structure-activity relationship (SAR) to provide an insight for the logical synthesis of more effective 1,2,4-triazole antifungal candidates. The diagram of choosing publications and the content of this review are illustrated in
Figure 1. Chart related to the content of provided in this review.1,2,4-triazole and 1H-1,2,4-triazole and 1H-1,2,4-triazole (Scheme 1) [32]. Tautomeric forms of the 1,2,4-triazole structure. A simple
method for preparing 1,2,4-triazoles has been introduced from the reaction of 1,2,4-triazoles from hydrazines. A series of 1,3-disubstituted-1,2,4-triazoles were synthesized by reacting amidine and trialkyl amines with K3PO4 as a base in the
presence of a copper (II) catalyst (Scheme 3) [34]. Synthesis of 1,2,4-triazole from amidine.I2-mediated oxidative N-S and C-N bond formations.1,5-Disubstituted-1,2,4-triazole from isothiocyanates (Scheme 4) [35]. I2-mediated oxidative C-N and N-S bond formations.1,5-Disubstituted-1,2,4-triazole from amidine.I2-mediated oxidative N-S and C-N bond formations.1,5-Disubstituted-1,2,4-triazole from amidine.I2-media
triazoles were prepared using copper (II) as the catalyst. This regioselective method makes it simple to produce 1,2,4-triazoles from aliphatic
amines and hydrazones has been developed using a cascade C-H functionalization, oxidative aromatization sequence, and double C-N bond formation under reflux circumstances in pyridine, 1-aryl-1,2,4-1H-triazole is arylated by an aryl
halide with electron-withdrawing groups using CuO as the catalyst (Scheme 7) [38, 39]. Arylation reactions of 1,2,4-triazole is alkylated at the N1 position, yielding in a mixture of 1-methyl- and 4-methyl-1,2,4-triazole with methyl sulfate alkylation in NaOH (Scheme 8) [40].
Alkylation reactions of 1,2,4-triazoles. A group of 4-Arylsubstituted-1,2,4-4H-triazoles yields via the reaction of N, N-diformylhydrazine with N, N-diformylhydrazine [42, 43], as
well as downloading via slight changes in amino heterocycles containing 3-amino-1,2,4-4H-triazoles in 1885 [31]. The primary procedures, such as the reaction of formamide with formylhydrazine, produced low yields of 1,2,4-triazoles in 1885 [31].
triazole [47, 48]. Later, it was found that condensation of formamide with hydrazine sulfate yielded 1,2,4-triazoles as antifungal [42, 49, 50] have been observed which included fluconazole, ravuconazole, ravucon
1,2,4-triazole-based drugs are under clinical use for the treatment of different diseases. Some of the most effective drugs available in the market are described in the following Table 1. Chemical structures of some bioactive 1,2,4-triazole-based marketed drugs. Pharmacological properties and clinical implications of all marketing antifungal
drugs.Drug/PubChem IDChemical nameAction of antifungalRef.Itraconazole, CID: 552832-Butan-2-yl-4-[4-[4-[(2R,4S)-2-(2,4-dichlorophenyl)-1,2,4-triazol-3-onTreatment of onychomycosis and seborrheic dermatitis[5153]Fluconazole, CID: 33652-(2,4-dichlorophenyl)-1,2,4-triazol-3-onTreatment of onychomycosis and seborrheic dermatitis[5153]Fluconazole, CID: 33
Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl) propan-2-olEffect on blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, dermatophytosis, and pityriasis versicolor[54, 55]Isavuconazole, CID: 69184854-[2-[(2R,3R)-3-(2,5-Difluorophenyl)-3-hydroxy-4-(1,2,4-triazol-1-yl) butan-2-yl]-1,3-thiazol-4-yl] benzonitrileTo treat invasive
yl]methoxy]phenyl]piperazin-1-yl]phenyl]-2-[(2S,3S)-2-hydroxypentan-3-yl]-1,2,4-triazol-3-oneFor the treatment of Scedosporium and fusarium species of pharyngeal candidiasis (OPC), including OPC retrofitting in the treatment of itraconazole and/or
fluconazole[6166]Voriconazole, CID: 71616(2R, 3S)-2-(2, 4-Difluorophenyl)-3-(5-fluoropyrimidin-4-yl)-1-(1, 2, 4-triazol-1-yl) butan-2-olTreatment includes candidiasis, coccidioidomycosis, histoplasmosis, penicilliosis, aspergillosis, and infections by Scedosporium or fusarium[6770]Albaconazole, CID: 71616(2R, 3S)-2-(2, 4-Difluorophenyl)-3-(2, 4-Difluorophenyl)-3-(2, 4-Difluorophenyl)-3-(2, 4-Difluorophenyl)-3-(3, 4-Difluorophenyl)-3-(
hydroxy-4-(1, 2, 4-triazol-1-yl) butan-2-yl] quinazolin-4-oneTreatment of antiprotozoal agent[71]Ravuconazole, CID: 4678254-[2-[(2R, 3R)-3-(2, 4-Difluorophenyl)-3-hydroxy-4-(1, 2, 4-triazol-1-yl) butan-2-yl] penzonitrileLimited activity against species of Scedosporium, fusarium, and zygomycetes[7274]Propiconazole, CID: 432341-[[2-(2R, 3R)-3-(2, 4-Difluorophenyl)-3-hydroxy-4-(1, 2, 4-Difluorophenyl)-3-hydroxy-4-(1, 
(2,4-Dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1,2,4-triazoleIn terms of agriculture as a systemic fungicide grown in meadow plants for seeds and aesthetic value, sports, wheat, mushrooms, corn, wild rice, peanuts, almonds, sorghum, oats, pecans, apricots, peaches, nectarines, plums, and prunes are used[75, 76]Fosravuconazole, CID:
9807507[(2R,3R)-3-[4-(4-Cyanophenyl)-1,3-thiazol-2-yl]-2-(2,4-difluorophenyl)-1,2-triazol-1-yl)butan-2-yl]oxymethyl dihydrogen phosphateTreatment of eumycetoma[31, 77]Fosfluconazole, CID: 214356\{[2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)propan-2-yl]oxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy2-yloxy
acidTreatment and prevention of superficial and systemic fungal infections[78]Flusilazole, CID: 736751-{[Bis(4-fluorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(1H, 1,2,4-triazoleUsed to control fungal infections in a variety of fruit and vegetable products[7981]Tebuconazole, CID: 86102(RS)-1-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chlorophenyl)-4,4-dimethyl-3-(4-Chloropheny
olUsed in agriculture to treat pathogenic fungi of plants[82]Triadimefon, CID: 393851-(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-oneUsed in agriculture to control various fungial diseases[83]Metconazole, CID: 862105-[(4-Chlorophenoxy)-1-(4-
fungal infections including Alternaria, rust, fusarium, and Septoria[84]Paclobutrazol, CID: 158076(2RS,3RS)-1-(4-Chlorophenyl)-4,4-dimethyl-2-(1,2,4-triazol-1-yl)pentan-3-olPlant growth inhibitor, triazole fungicide, root growth, and drought stress resistance can be used as a chemical method to reduce the risk of habitat in cereal
crops[85]Myclobutanil, CID: 63362-(4-Chlorophenyl)-2-(1,2,4-triazol-1-ylmethyl)hexanenitrileUsed as a fungicide which is a steroid demethylation inhibitor, specially inhibiting ergosterol biosynthesis[86, 87]Fluconazole is well known as one of the most potent antifungal drugs with remarkable interest in medicinal chemistry. Due to the importance of
fluconazole as a reference drug, the structure-activity relationship is shown in Figure 3. Structure-activity relationship of fluconazole. This part of the review is classified into two parts based on the structural similarities of 1,2,4-triazole drugs and then discussed 1,2,4-triazole drugs are drugs and then discussed 1,2,4-triazole drugs are drugs and then discussed 1,2,4-triazole drugs are drugs are drugs and the drugs are drugs
triazole-based scaffolds with various functional groups such as indole, denominated more antifungal properties, as well as SARs of all synthesized compounds. Most triazole compounds containing 1,2,3-benzotriazine-4-one demonstrated more antifungal
activity against Candida albicans and Cryptococcus neoformans than reference drug with MIC values ranging from 0.0156 to 2.0g/mL. Furthermore, a strong SAR investigation revealed that derivatives with groups at the 5-, 6-, and 8-positions. In
addition, products containing halogens such as Cl and F demonstrated more excellent antifungal activity specifically against Aspergillus fumigatus (MIC = 0.25g/mL) and moderate activity against fluconazole-resistant
Candida albicans strains (Figure 4) [88]. The structure of 1, 2, 3-benzotriazin-4-one. Blokhina et al. [29] investigated the fungicidal activity of thiazole (1,5-d) pyrimidine hybrids with (1H-1,2,4) triazole. All derivatives include the methyl-(2a), fluoro-(2b), and chloro-(2c) substituents at the para position. In vitro evaluation of various compounds with a
potent alkylpiperazinyl linker demonstrated antifungal activity similar to the standard drug. The most active compounds are methyl-(2a), fluoro-(2b), chloro-(2c) methyl-(3a), and fluoro-(3b). Based on MIC values, antifungal activity is classified as poor (32g/mL), modest (1632g/mL), good (48g/mL), excellent (0.062g/mL), or outstanding based on MIC
values (Figure 5). Antifungal screening of novel hybrids of triazole derivatives. Montoir et al. [89] reported a novel class of azole antifungal compounds demonstrated fungicidal activity against pathogenic Candida species in vitro (fluconazole susceptible and fluconazole resistant) and
were more active than voriconazole against two Candida albicans candidates. Compound 4e also showed promising in vitro activity against several filamentous fungi, including Aspergillus fumigatus (Figure 6). Chemical structure of novel azole antifungals containing a fused triazinone scaffold. Xie et al. [90] demonstrated that the entire series of
triazole containing isoxazole compounds (5a-f) were antifungal against eight human pathogenic fungi. Compound 5a showed a strong inhibitory activity toward Candida albicans with MIC80 values of 0.0313g/mL. According to the SARs study, mono-fluorine on the phenyl ring possesses antifungal activity. On the other hand,
enhancing the number of fluorine atoms (5c-d) may result in a reduction in antifungal activity (Figure 7). Chemical structure of novel triazole analogues featuring isoxazole moieties. In comparison to the reference drugs, voriconazole, and ravuconazole, and ravuconazole, and ravuconazole analogues featuring isoxazole moieties. In comparison to the reference drugs, voriconazole, and ravuconazole, and ravuconazole, and ravuconazole analogues featuring isoxazole moieties.
fungicidal activity against eight human pathogenic fungi, with particularly noticeable activity against ell the investigated fungi with (MIC80 = 0.01560.5mg/mL), which is greater than fluconazole and ravuconazole. SAR study shows that para fluoro (6e,
6h), para chloro (6b), and para cyano (6c) substituted phenylalkynyl, or pyridinyl alkynyl (6m, 6n) side chains improve activity. Compounds with R groups in the para position are shown to be more active than meta or ortho compounds with R groups in the para position are shown to be more activity.
derivatives toward 16 Candida isolates from five different species, including fluconazole-susceptible and fluconazole-susceptible and fluconazole-susceptible isolates; significantly, compounds 7b and 7e
were also active against fluconazole-resistant species. However, the effect of chloro substitution depends on the type of species. For example, the 2,4-dichloro substitution depends on the type of species. For example, the 2,4-dichloro substitution depends on the type of species. For example, the 2,4-dichloro substitution depends on the type of species. For example, the 2,4-dichloro substitution depends on the type of species. For example, the 3-chloro substitution depends on the type of species. For example, the 2,4-dichloro substitution depends on the type of species.
substituents. The addition of fluoro or bromo groups to the benzyl regioisomers (7f-h), the 3-fluoro 7g analog was more active against Candida species (Figure 9) [92]. Benzylthio analogues of fluoroazole. Chandrika et al. [93] investigated novel fluoroazole (FLC) compounds for
antifungal activity against the clinical strains of C. parapsilosis, C. glabrata, and Candida with aryl, alkyl, cycloalkyl, and dialkyl-amino FLC derivatives was shown to be directionally related to the length of the alkyl chains (Figure 10). The study of antifungal
properties in new fluconazole derivatives. Tekale et al. [94] investigated the antifungal activities of triazole compounds, including imidazole. The impact of the imidazole side chain on the in vitro fungicidal activity of novel synthesized compounds toward various microorganisms such as aspergillus, niger, aspergillus fungicidal activity of novel synthesized compounds.
was demonstrated. Compound 9e had the lowest activity against C. albicans, and compounds 9b & 9d had higher activity against A. niger than the other compounds containing 1,2,3-triazoles or substituted amines as side chain 10a-o
derivatives demonstrated better antifungal properties than those of fluconazole on three significant fungal infections except for 10i. Furthermore, the considerable compounds 10d, 10k, 10n, 10m, and 10o were reported on the Aspergillus fungities fundamental fungal infections except for 10i. Furthermore, the considerable compounds 10d, 10k, 10n, 10m, and 10o were reported on the Aspergillus fundamental fungal infections except for 10i. Furthermore, the considerable compounds 10d, 10k, 10n, 10m, and 10o were reported on the Aspergillus fundamental fundam
Aspergillus spp. In vitro biological assessment of new triazole derivatives. Sadeghpour et al. [96] reported two classes of novel fluconazole-derivatives containing nitrotriazole or 2-(piperazin-1-yl) ethanol moieties, which were evaluated for
antifungal activity against standards and clinically isolated yeasts, and their MIC structures were compared with those of fluconazole. Nitrotriazole derivatives 11a-d and compounds 12g and 11b containing two chlorine atoms exhibited good activity against the tested fungus, notably some fluconazole-resistant species. Compounds 11a, 11b, and 12g
with 2,4-difluorophenyl or 2,4-dichlorophenyl or 2,4-dichlorophenyl groups had more excellent antifungal activities of new triazole derivatives of ravuconazole were demonstrated against eight fungal isolates. Compounds 13e (2-difluorophenyl groups had more excellent antifungal activities of new triazole derivatives bearing nitrotriazol or 2-(piperazine-1-ylFig) ethanol moieties. In vitro antifungal activities of new triazole derivatives bearing nitrotriazol or 2-(piperazine-1-ylFig) ethanol moieties. In vitro antifungal activities of new triazole derivatives bearing nitrotriazol or 2-(piperazine-1-ylFig) ethanol moieties. In vitro antifungal activities of new triazole derivatives bearing nitrotriazol or 2-(piperazine-1-ylFig) ethanol moieties. In vitro antifungal activities of new triazole derivatives bearing nitrotriazol or 2-(piperazine-1-ylFig) ethanol moieties.
F), 13f (2, 3-diF), and 13g (2, 4-diF) in particular displayed activity to ravuconazole, demonstrating that the 2,4-diflourophenyl group is more active than the 2,5-diflourophenyl group is more active than the 2,4-diflourophenyl group is more active than the 2,5-diflourophenyl group. Compounds without a fluoro substitution on the phenyl ring, such as 13a (4-CH3), 13c (4-SO2-CH3), 13b (4-NO2), and 13d (4-CN), were less active than those with
fluorophenyl groups, such as 13k (2, 6-diF), 13h (2, 5-diF), and 13l (2, 4, 6-triF) (Figure 14) [97]. New triazole derivatives of ravuconazole and isavuconazole and isavuconazole and isavuconazole and isavuconazole and isavuconazole.
Furthermore, compounds 14j, 14k, 14l, 15a, and 15b (MIC = 0.1250.5g/mL) were shown to be more effective than fluconazole (MIC = 0.25g/mL) against C. glabrata. SARs revealed that 3-substitutions (14b, 14c), while electron-rich thiophene (14h, 14i) significantly outperformed the
electron-deficient pridinyl group in antifungal activity (14g). Antifungal activity may be enhanced by replacement of the phenyl group of compound 14a by a cyclopertyl (14k), and cyclopertyl (14g). Structure of triazole-
piperdine-heterocycle.Compared to fluconazole and 5-flucytosine, the new fungicidal hybrids of 5-flucytosine and fluconazole showed modest antifungal activity. Surprisingly, a hybrid of 3,4-dichlorobenzene can inhibit clinical-resistant strain C. albicans and the growth of C. albicans ATCC 90023 with MIC values of 0.02 and 0.008mM, respectively.
Compound 16e inhibited C. albicans rapidly, whereas compound 16a lacked fungicidal activity due to the lack of substituents on the phenyl ring (ure 16) [99]. Structure of novel triazole derivatives having -lactam that were screened for antifungal activity against six
pathogenic fungi in vitro. Furthermore, the pyridyl- and phenyl-substituted compounds 17d and 17e showed moderate antimicrobial activity against Cryptococcus neoformans and Candida spp. (Figure 17). Novel triazole derivatives bearing -lactam. Zhang et al. [101] reported the triazole sequence as a miconazole analogue with antifungal against five
fungi. Among these compounds, 18b, 3,4-dichlorobenzyl had the highest activity. Furthermore, the antifungal activity of 3,4-dichlorobenzyl micronazole analogue 18e (MIC=16g/mL), due to F or Cl may be significantly improved over nitro group
important fungal pathogens was investigated. Particularly, 19g (MIC = 0.031g/mL) and 20b (MIC = 0.031g/mL) and 20a had greater activity (MIC 0.125g/mL) than fluconazole (MIC = 0.25g/mL). Additionally, the presence of pridinyl
group (19a and 19l) 1,2,4-oxadiazole derivatives reduces antifungal activity. On the contrary, compound 19n with furan demonstrated better activity than compound 19n with substitutions on the phenyl ring that revealed distinct effects on antifungal activity. Furthermore, 4-methoxyl (19f), 4-fluoro (19h), and 4-trifluoromethyl (19g) alterations
demonstrated promising antifungal activity, with 19g showing the most activity against C. albicans (MIC = 0.031g/mL). Surprisingly, compound 19c exhibited significant fungicidal activity. In contrast, the antifungal activity against C. albicans (MIC = 0.031g/mL).
oxadiazole derivatives such as 20f, 20i, and 20j demonstrated modest antifungal activity. Finally, the heterocyclic pyridinyl derivative 20a demonstrated the greatest activity (Figure 19) [102]. Structure-activity relationship between triazole alcohols bearing
N-(halobenzyl) piperazine carbodithioate scaffold as effective antifungal agent in vitro bioassays versus C. albicans, C. parapsilosis, C. krusei, and C. tropicalis in which the best activity indicated N-(4-chlorobenzyl) derivative 21b with MIC values of 0.0630.5mg/mL, being several times more effective than fluconazole. Furthermore, the 3-
chlorobenzyl compound 21a displayed a good activity toward both albicans and non-albicans species of Candida. Generally, according to MICs, 2, 4-difluorophenyl derivatives were more active than their dichlorophenyl compounds. In addition, SAR studies revealed that 2,4-difluorophenyl-carbinol was higher than the 2, 4-dichlorophenyl-carbinol
scaffold. Moreover, assessment against fluconazole-resistant isolates showed that compound 21b was active against C. albicans, C. krusei, and C. parapsilosis isolates, with MIC values of 2 to 16mg/mL (Figure 20). Triazole alcohols holding N-benzylpiperazine carbodithioate moiety. Ciprofloxacin and itraconazole were employed to screen 1,2,4-triazole
derivatives fused with novel benzene-ethanol which were assessed at concentrations ranging from 0.125 to 64mg/mL. Furthermore, compounds 22a, 22g, and 22i showed much better growth inhibitory activity, like substituent
groups on the para and ortho positions of a benzene ring, can be effective in antifungal activity (Figure 21) [104]. Novel benzene-ethanol bearing 1,2,4-triazole derivatives. A class of 1,2,4-triazole derivatives has been tested toward Magnaporthe oryzae. Aromatic ring structures revealed that the methyl group at position 1,4 of the phenyl ring 23b and
the phenyl moiety at the para position of phenyl 23c reduced antifungal activity. When an electron-withdrawing group (trifluoromethyl group) had a positive efficacy on increasing the antifungal activity of this synthetic series (comparison of
antifungal activity 23b with 23f). The introduction of two chlorine atoms to the phenyl moiety had a distinct effect on increased the antifungal activity. Compound 23h with the 2,4-dichlorophenyl analogue notably reduced the antifungal activity. The mono
chlorine substitution at position 4 of the phenyl ring (23i) reduced the antifungal activity of these synthesized derivatives. According to the phenoxy moiety (ring B) such as 24a, 24b, and 24c
can lead to an increase in antifungal activity. As a result, the fungicidal activity of the analogue without a chlorine substituent at ring B (24j) was the most effective against M. oryzae among these compounds (Figure 22) [105]. 1-(4-Phenoxymethyl-2-phenyl-[1, 3] dioxolan-2-ylmethyl)-1H-1,2,4-triazole derivatives. Al-Wabli et al. [106] estimated the
antifungal characteristics of a variety of novel indole-triazole compounds. The MIC value of compounds 25f, which included N-phenyl and 3,4-dichlorobenzyl moieties, was 2mg/mL against Candida albicans. In addition, the para benzyl substituent exhibits antifungal activity. Also, MIC values for compounds 25b, 25c, 25d, 25e, 25f, and 25g having a
phenyl moiety on the triazole ring are 250500g/mL against Bacillus subtilis. Meanwhile, compounds 250, 25p, and 25q with an N-cyclohexyl substituent showed moderate to good activity toward the tested Candida albicans strain (Figure 23). Evaluation of the antifungal activity of new indole-1,2,4-triazole conjugates. The nortopsentin analogues
containing 1,2,4-triazole demonstrated good antifungal activity. Compounds 26d, and 26f were more fungicidal toward Cercospora arachidicola Hori than chlorothalonil and carbendazim (commercial fungicidaes). Compounds 26d and 26f indicated better actions against most of the fourteen plant pathogens (Figure 24) [107]. 1,2,4-Triazole
derivatives containing nortopsentin. According to the study by Ahuja et al. [108], compound 27c has a lower ED50 value than the triazole fungicide propiconazole. Significantly, compound 27c showed the highest activity compared with other experimental fungi, with an ED50 value of 16 to 21g/mL, which is higher than the ED50 values of the standard
commercial fungicides used (tilt: 2025g/mL and carbendazim: 150230g/mL (Figure 25). Benzimidazole-1,2,4-triazole hybrid compounds 28m, 28n, 28f, and 28g had good fungicidal activity (MIC50 values of 0.78 to 1.56g/mL) because of the presence of a fluoro or chloro substituent at
the C-para position of phenyl, whereas compounds 28c, 28a, and 28b did not. Compounds 28c, 28a, and 28b did not. Compounds 28c demonstrated adequate fungicidal activity with reference drugs fluconazole and ketoconazole. As a result, chloro or fluoro substitution at the C-5 position of
benzimidazole is vital and could have had a significant influence on antifungal activity (Figure 26) [109]. SAR outline of the benzimidazole-triazole hybrid compounds. The benzimidazole hybrid compounds showed moderate antifungal activity toward Candida krusei (ATCC 90030), Candida albicans (ATCC 24433),
and Candida parapsilosis (ATCC 22019), with MIC50 values ranging from 12.5 to 0.78mg/mL. The findings revealed that compound 3,4-dihydroxy has an influence on the activity (Figure 27) [110]. Structure of new benzimidazole-triazoles. Novel tri-substituted 1,2,4-triazoles containing benzimidazole were tested for antifungal efficacy against three
plant pathogenic fungus, and compounds 30e and 30g showed potent activity against Venturia nashicola. However, 30d and 30f indicated sufficient activity against Fusarium graminearum (Figure 28) [111]. Tri-substituted 1,2,4-triazoles containing benzimidazole moiety. Luo et al. [112] reported a new group of benzimidazole-derived triazoliums and
naphthalimide triazoles that have been thoroughly tested for antifungal activities. Triazoliums 31g and 31f with 3-fluorobenzyl moiety demonstrated the highest antifungal activity (MIC = 219mg/mL) showed more efficacy than
fluconazole (MIC = 7230mg/mL). Furthermore, bis (4-fluorobenzyl) triazolium 31b (MIC = 419mg/mL) displayed high activity relationships between benzimidazole-derived naphthalimide triazoles. The antifungal efficacy of 1,2,4-triazoles having quinoline
moiety against A. fumigatus and Candida albicans was highest owing to methoxy and chloro substituents. As a result, 32e, 32g, and 32m derivatives with methoxy and chloro substituents had the highest enhanced activity (Figure 30) [113]. 1,2,4-Triazole hybrids of 2-(aryloxy) quinolones. D'Souza et al. [114] investigated the fungicidal of new quinoline
triazoles. Compounds 33b and 34b with chlorine substituents on the aromatic ring demonstrated more antifungal activity evaluation of quinolone-triazole derivatives. Fan et al. [115] investigated the antifungal activity of 1,2,4-triazolo [4,3-a]pyridine-containing
quinazoline thioether derivatives at 50mg/mL. Except for compound 35c against the fungi Verticillium dahlias and Fusarium oxysporum (inhibition rates of 65.4 and 52.5%, respectively), all of these compounds failed to demonstrate apparent fungicidal activity (45%) against the pathogen V. dahliae (46.8%) against the fungi Verticillium dahlias and Fusarium oxysporum (inhibition rates of 65.4 and 52.5%, respectively), all of these compounds failed to demonstrate apparent fungicidal activity (45%) against the pathogen V. dahliae (46.8%) against the fungi Verticillium dahlias and Fusarium oxysporum (inhibition rates of 65.4 and 52.5%, respectively), all of these compounds failed to demonstrate apparent fungicidal activity (45%) against the pathogen V. dahliae (46.8%) against the fungicidal activity (45%) against the fungicid
(Figure 32). Quinazoline thioether-1,2,4-triazole fungicidal activity of quinazolin-containing 1,2,4-triazoles against six significant phytopathogenic fungi in agriculture. Furthermore, compounds 36h and 36g were showed a remarkable fungicidal activity toward Gloeosporium fructigenum at
50mg/mL, comparable to the commercial antifungal hymexazol (Figure 33). 1,2,4-Triazole containing quinazoline derivatives indicated in vitro antifungal activity against ten fungal strains except C. neoformans. Nevertheless, 37a and 37b exhibited activity only against A.
niger and A. fumigatus. Compounds 37c, 37d, 37e, 37f, and 38b revealed excellent fungicidal activities against A. fumigatus (MIC = 0.49g/mL). In contrast, 38b had stronger inhibition with respect to the reference drug toward S. racemosum (MIC = 0.49g/mL) and 37e
confirmed similar activities to amphotericin B (MIC = 0.490.98g/mL). In addition, compounds 37c-37e, 38a, and 38b showed the highest activity versus G. candidum (MIC = 0.490.98g/mL) as compared with amphotericin B (MIC = 1.95g/mL) (Figure 34) [117].
investigated the antifungal activities of 1,2,4-triazolos [4,3-a]-quinoxaline derivatives with various substituted pyrazole moieties at position 4. When compared with the reference clotrimazole (MIC = 12.5g/mL), compounds 39, 41a, and 41b inhibited only
weakly (MIC = 50g/mL) growth against the same organism. Clotrimazole activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 42. Regarding the activity against the fungus A. fumigatus was reduced by one-quarter in studies 39 and 40 and
6.25g/mL) (Figure 35). Antifungal study on pyrazol-1,2,4-triazole quinoxalines. Yang and Bao [119] demonstrated that 1,2,4-triazole derivatives (43a-43k) containing N-(substituted phenyl) acetamide and the quinazolinylpiperidinyl moiety group did not exhibit remarkable inhibition activity against phytopathogenic fungi such as Phytophthora infestans,
Verticillium dahliae, and Gibberella zeae) at 50mg/mL save compounds 43e and 43k that showed modest inhibitory activity against the fungus G. zeae (Figure 36). 1,2,4-Triazole derivatives containing the quinazolinylpiperidinyl moiety. Sompalle et al. [120] investigated the antifungal activity of a class of 1,2,4-triazole-quinazolinethiones (44a-l) against
Aspergillus niger (A. niger) and Aspergillus flavus (A. flavus) in combination with the commonly used antifungal drug fluconazole (Figure 37). SAR study of triazolo-quinazolinethiones. All triazole derivatives with N-alkylated groups were tested for fungicidal activity toward Candida albicans and Aspergillus flavus (and anthelmintic activity against
 Pheretima posthuma, and the compound containing group CH3 at the ortho position of the phenyl ring showed good inhibition with a standard antifungal drug, Nystatin, while the antifungal activity of the other structures was lower (Figure 38) [121].
Structure of triazole derivatives containing N-alkylation. Jin et al. [122] investigated the fungicidal activity of novel compounds containing 1,2,4-triazole with different substituted groups toward Gibberlla nicotiancola, Pythium solani, Gibberlla saubinetii, and Fusarium oxysporum f.sp. niveum in vitro. Compound 46 had good activity against the case
fungus, indicating that 1,2,4-triazole-imidazole can contribute to antifungal properties. Methyl at position Q increased the activity, the activity order is 47>46, and compound 47 demonstrated a remarkable antifungal activity. As a result, positions P and Q may have an impact on the activity at the same time (Figure 39). Chemical structure of novel
1,2,4-triazole derivatives.1,2,4-Triazole derivatives with a pyrimidine moiety were evaluated for fungicidal activity against Phompsis sp. that was even better than pyrimethanil (32.1mg/mL). Compound 50d, on the other hand, had higher activity against B. cinerea and B. dothidea with
55.1 and 40.1mg/mL, respectively, when compared with Pyrimethanil (57.6 and 62.8mg/mL) (Figure 40) [123]. The structure of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety and a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety and a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety and a pyrimidine moiety. Antifungal evaluation [1, 2, 4] of triazole derivatives with a pyrimidine moiety and a pyrimidine moiety
griseofulvin (MIC 500mg/mL) against C. albicans. Surprisingly, the substituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted or diversely para-substituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted or diversely para-substituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted phenyl ring was responsible for variable biological results, while the triazole with nonsubstituted phenyl ring was responsible for variable biological results.
In addition, the compounds having OCH3 group substitution (compound 51f) effectively showed poor inhibited the E. coli bacterial strains, although the derivative with the electron-withdrawing group such as NO2 (compound 51i) efficiently inhibited the E. coli bacterial strain
as well as was found potent toward the C. albicans strain. Finally, compound bearing heteroaryl substitution (compound 51l) led to the improvement in the activity against the E. coli strain (Figure 41) [124]. [1, 2, 4] Triazolo [5,1-b] quinazolin-8(4H) derivatives. All 1,2,4-triazole having amine derivatives were evaluated and shown to be effective in
inhibiting fungal pathogens with MIC values ranging from 1 to 256g/mL. They were proposed as the potential antifungal agents that synthesized under optimized conditions as 3(5)-substituted 1,2,4-triazol-5(3)-amine 52. As starting materials, however, several heteroaryl hydrazides and aryls were used as starting materials (Figure 42) [125]. Study of
1,2,4-triazole derivatives. Appna et al. [126] described the fungicidal activity of novel 1,2,4-triazole fused pyrido [2,3-d] pyrimidine derivatives (53a-d and 54a-c) against different Candida strains. The antifungal activities of the synthesized compounds 53d, 54b, and 54c were shown. SAR investigations revealed that trifluoromethyl, fluoro, bromo, and
nitro groups on the furyl and phenyl rings of pyrido [2,3-d] pyrimidine could increase antifungal activity. As well, 4-nitrophenyl triazole in combination with 2-furyl pyrido [2,3-d] pyrimidine (54b) exhibited the
same activity. The antifungal effects of 2-chloro-4-fluoro phenyl triazole with 2-phenyl pyrido [2,3-d] pyrimidine (53d) were favorable (Figure 43). Chemical structure of new 4-hydrazone functionalized/1,2,4-triazole derivatives were synthesized by Singh et al. The antifungal
characteristics of the compounds showed that most of them could effectively inhibit the growth of the tested fungal strains. However, none of them were superior to the reference drug fluconazole. Compound 55l had the most potent antifungal activity against both fungi. 55l revealed comparable activity (A. niger: MIC = 11.7M; C. albicans: MIC =
10.9M) with the reference fluconazole (A. niger: MIC = 9.4M; Candida albicans: MIC = 10.2M). Apart from that, antifungals 55f (A. niger: MIC = 15.6M; C. albicans: MIC = 14.1M) and 55a (A. niger: MIC = 28.1M; C. albicans: MIC = 14.1M) and 55a (A. niger: MIC = 14.1M) and 55a (A. niger: MIC = 10.2M).
[128] investigated the antifungal effects of a variety of 4-amino-5-substituent-1,2,4-triazole-3-thione Schiff bases toward Pythium solani, Gibberlla nicotiancola, Gibberlla 
toward Gibberlla saubinetii and Gibberlla nicotiancola than triadimefon. The antifungal activity of 56a-d and 57a-d analogues was tested against four plant pathogenic fungi, including Pythium solani, Fusarium oxysporium f.sp. niveum, Gibberlla nicotiancola, and Gibberlla saubinetii (Figure 45). Chemical structure of new 1,2,4-triazole Schiff base
derivatives. Zhang et al. [129] displayed a new class of piperazine-containing 3-(furan-2-yl)-1,2,4-triazole important in vitro fungicidal activity toward a variety of test fungi. Compounds 58g, 58f, and 58h having R1 = CF3 performed
better than others (R1 = F or Cl). In comparison, the SARs of the compounds revealed 2-position of substituted benzylideneamino and ortho position of substituted benzylideneamino and ortho position of substituted benzylideneamino and ortho position of phenylpiperazine, where a large group would be favorable for higher fungicidal activity. Finally, compounds with an EWG at the benzyl ring position or an electron-donating group
at the 2,4-position of the benzene ring, such as 58b and 58a, demonstrated higher activity (Figure 46). Study of the structure of new piperazine-bearing 3-(furan-2-yl)-1, 2, 4-triazole. Trialkylamine compounds having a triazole moiety were evaluated in vitro for antifungal activity against six phytopathogenic fungi at 50mg/mL (Magnaporthe grisea
Curvularia lunata, Alternaria solani, Fusarium solani, Fusarium solani, Fusarium solani, A. alternata, and F. graminearum). Compounds 59k (3-F), 59m (3,4-diCl), and 59d (2-Br) showed good antifungal activity against F.
graminearum with EC50 values of 11.60, 5.14, and 16.24mg/mL, respectively. Also, electron-donating groups 590 (Me) or 59p (OMe) considerably reduced the activity. In contrast, the presence of halogen atoms such as 59k (3-F), 59c (4-Cl), (3,4-diCl), and 59n (4-Br) might increase the activity (Figure 47) [130]. Structure of trialkylamine derivatives
bearing a triazole moiety.1,2,4-Triazole-pyridine products with hydrazone scaffold (compounds 60a-60h) were tested in vivo at 100mg/mL against Stemphylium lycopersici (Enjoji) Yamamoto (SL) and Fusarium oxysporum sp. Cucumebrium (FO).
60e (p-N (CH3)2), 60b (p-F), 60f (p-CF3), and 60g (p-CH3) demonstrated strong antifungal activities. As a result, the furan ring-substitution exhibited more activity against SL and FO (Figure 48) [131]. (SAR) analysis
of 1,2,4-triazolo-pyridine derivatives containing hydrazone moiety. Remarkable antifungal activity of a number of new 1,2,4-triazole derivatives against different strains of Aspergillus fumigatus, Candida albicans, and Candida crocus has been reported in comparison with those of commercial fungicides ketoconazole and itraconazole. All of the
derivatives investigated, the dichloro urea analogue and bromo substituted triazole, stand out as the most favorable compounds. The most potent compounds against A. fumigatus were 64l, 61b, 61a, and 61c, with MIC values ranging from 0.114 to 0.230mol/mL. Instead, amide analogues such as 62f can influence the activity, with the amide moiety 62f
having higher activity than less bulky triazoles such as 650 and 65p. Furthermore, compound 63h with the sulfonamide substitution is responsible for the activity, being several times more potent than ketoconazole. Conversely, these derivatives were less active than itraconazole (Figure 49)
[132]. The study of antifungal properties of 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (66), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (66), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (66), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (68), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (68), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (68), 4-thiazolidinone (67), and 1,2,4-triazoles. Dincel et al. [133] screened a group of novel hydrazinecarbothioamide (68), 4-thiazolidinone (68), 4-thiazolidinon
and T. mentagrophytes var. echinacea. Generally, 1,2,4-triazole-3-thiones and 4-thiazolidinones showed better fungicidal activity rather than thiosemicarbazide derivatives. As a result, the 3-allyl substitution of 4-thiazolidinones is critical for their antifungal activity. Compounds 67d (R = CH2-CH = CH2), 68c (R = C3H7), and 68d (R = CH2CH = CH2)
had the highest fungicidal activity against S. aureus (MIC = 32g/mL). Also, 68c (R = CH2CH = CH2) showed the greatest activity towards P. aeruginosa (MIC = 32g/mL) (Figure 50). Structure of hydrazinecarbothioamides, 4-
thiazolidinones, and 1,2,4-triazole-3-thiones. Cheng et al. [134] investigated the fungicidal activity of new groups of 1,2,4-triazole benzoyl aryl amines. The findings revealed a clear relationship between the structure and training in these compounds as well. The electron-withdrawing group oi-pr(isopropyl) at the para position has a favorable impact or
high activity, and the preferred groups were alkoxy carbonyls. This compound indicated the most effective fungicidal activities with EC50 values of 0.12, 0.19, and 0.01mg/mL against S. sclerotiorum, F. graminearum, and G. graminis var. tritici, respectively. Alkoxy carbonyls revealed the highest activities (69a-b and 69c-g). In
contrast, no significant increase in the activity was observed when more than one electron-withdrawing group was added to aniline. For instance, if the second electron-withdrawing groups such as CF3 or Cl were added to the meta situation of aniline, the activity against G. graminis var. tritici would be reduced (69e and 69f) (Figure 51). The
structure of 1,2,4-triazole benzoyl arylamine compounds. The evaluation indicated that all 1,2,4-triazole derivatives had fungicidal activity, with MIC values of 0.320.64mM) and ketoconazole (MIC values of 0.281.88mM). Compound 70c, having a MIC value of 0.020.04mM
exhibited the best antifungal activity rather than compound 70a (Figure 52) [135]. New vinyl-1, 2, 4-triazole analogues. Wu et al. [136] evaluated the fungicidal activity of a novel series of 1,2,4-triazole derivatives containing an amide moiety. Compounds 71a, 71d, 71e, and 71f had the highest antifungal activity against Botrytis cinerea. Meanwhile
compound 71b, when R was CH3, exhibited better antifungal property against Phomopsis sp., compared with that of pyrimethanil. SAR studies revealed that 4-pyridine in the R substituent group and the smaller alkyl substituent groups (H or CH3) could have a favorable influence on the activity, such as 71a>71b>71c. Meanwhile, when R = OH is
added to the 4-positions of phenyl and substituted phenyl, the action against Phomopsis sp., B. dothidea, and B. cinerea rises in the sequence 71d>71g>71k. Furthermore, when R=4-pyridine, the action against Phomopsis sp., B. dothidea, and B. cinerea were higher than those of compound 71e (R
2-pyridine) (Figure 53). 1,2,4-Triazole derivatives bearing an amide moiety. Yurtta and Cantrk [137] investigated triazole-oxadiazole compounds against C. krusei, C. glabrata, C. albicans, and C. parapsilosis and found that triazole-oxadiazole compounds against C. krusei, C. glabrata, C. albicans, and C. albicans, and C. parapsilosis and found that triazole-oxadiazole compounds against C. krusei, C. glabrata, C. albicans, and C
62.5mg/mL). The oxadiazole rings of these derivatives differ due to the benzothiazole and phenyl rings linked to the acetamide molecule. Meanwhile, compounds 72e (R = NO2) and compounds .Li et al. [138] reported a group of N-
phenylacetamide containing 1,2,4-triazole derivatives (74a-f) that were screened in vitro for antifungal assessment, and specific compounds, such as 74b-f derivatives, inhibited the growth of the tested fungus. Among all synthesized compounds, 74a exhibited no antifungal activity. Moreover, mono-substituted halogen substituents in the benzene ring
in either the ortho or the para position, displayed antifungal activity (Figure 55). The study of N-phenylacetamide containing 1,2,4-triazole derivatives toward two Candida albicans strains (C. albicans ATCC 10231 and C. albicans ATCC 18804) and one non-Candidae
albicans strain (C. krusei ATCC 6258) were evaluated. Its antifungal activity was shown by the presence of a halogenated aryl substituent linked to the 3-mercapto group. Compounds 75d, 75f, and 75g had smaller MIC values than the other 1,2,4-triazolyl-thioethers, indicating that the 1,2,4-triazole-3-yl-mercapto derivatives with a 4-Cl-phenyl
component had more excellent antifungal activity against the Candida krusei ATCC 6258 strain. In this series, compound 75d in this series has the lowest MIC value (Figure 56) [139]. The chemical structures of 1, 2, 4-triazole-3-yl-mercapto derivatives. Antifungal activities of new myrtenal derivatives containing 1,2,4-triazole were tested against
Physalospora piricola, Fusarium oxysporum f.sp. cucumerinum, Cercospora arachidicola, Alternaria solani, and Gibberella zeae at 50mg/mL. Among these compounds, 76a (R = Et), 76c (R = i Pr), and 76e (R = o NO2 Bn) had the most significant antifungal activity against P. piricola. Among these derivatives, 76a (R = Et), 76c (R = i Pr), and 76e (R = o NO2 Bn) had the most significant antifungal activity against P. piricola.
NO2 Bn) indicated the highest antifungal activity against P. piricola (Figure 57) [140]. Novel myrtenal-based 4-methyl-1, 2, 4-triazole-thioethers. Cheng et al. [141] evaluated a series of 4,5-disubstituted-3-S-(-D-acetyl glycosyl)-1,2,4-triazole-thioethers. Cheng et al. [141] evaluated a series of 4,5-disubstituted-3-S-(-D-acetyl glycosyl)-1,2,4-triazole-thioethers.
50g/mL. Particularly, compounds 77c, 77g, 77n, and 77p displayed 6068.6% inhibitory rates against S. sclerotiorum, with the antifungal activity of R2 = ethyl being lower than those of the other compounds against S. sclerotiorum. In other
 words, compounds containing a galactosyl mojety, such as compound 77n, demonstrated highly favorable antifungal activity (Figure 58), 1.2.4-Triazole with glucosyl mojety compounds. Bitla et al. [142] synthesized and screened bis(1.2.3 and 1.2.4)-triazole with glucosyl mojety compounds.
derivatives for antifungal activity, and compounds 78a, 78d, 78f, and 78i had the highest activity. It is remarked that bromo and chloro substitutes at meta and para positions of the aryl ring were highly important. Compound 78f indicated superior activity against S. aureus MTCC 96 (MIC3.9 0.05g/ml) (Figure 59). Assessment of bis-1,2,4-triazole
derivatives as antifungal agents. Beyzaei et al. [143] synthesized and tested a new class of 1,2,4-triazole-3-thiones in glycerol/potassium carbonate and assessed them for antifungal infections. Fusarium oxysporum and Aspergillus fumigatus were inhibited with all of
them. The most excellent antifungal activities indicated triazole 79c that contains R = 4-nitrophenyl has the high-affinity binding to the receptor. Hydrogen bonds between the N-1 azole ring and some amino acid residues in the target enzyme interact predominantly. These findings might aid in the development
of antifungal drugs (Figure 60). Antifungal study on 4,5-substituted 1,2,4-triazole derivatives. Compounds 80a-d (Figure 61) in particular showed high antifungal activity. The relationship between biological activity and structure revealed that compounds
with the sulfur atom exclusively in the thiol form exhibited activity. Furthermore, compounds 80a and 80c, at a concentration of 1,2,4-triazole with a thiomethyl bridge. Sidhu and Kukreja [145] reported new compounds based on lead hybridization of 1,2,4-triazoles
with fluorinated benzothiazol-2-yl that were tested for fungicidal activity against P. striiformis, D. oryzae, and U. hordei in contrast with conventional fungicides. Furthermore, derivatives 81b and 81c are active against most of the experimental fungicides. Furthermore, derivatives 81b and 81c are active against most of the experimental fungicides.
respectively, against P. striiformis that was compared to the standard fungicide (EC50 value 0.10 of mmoles/L). Compound 81a has the greatest EC50 value (0.17mmoles/L) against U. hordei when compared to Vitavax (EC50 value 0.10 of mmoles/L) against U. hordei when compared to Vitavax (EC50 value 0.10 of mmoles/L).
new series of pyrazole bearing triazolo-thiadiazole derivatives (82a-1) which were evaluated to have antifungal activity versus A. Niger, C. albicans, and A. clavatus along with nystatin and griseofulvin as standard drugs. Amongst them, compounds 82b and 82j revealed good antifungal activity. Compound 82j has shown the most activity (Figure 63).
Chemical structures of pyrazole bearing triazolo-thiadiazole derivatives. The antifungal activity of 1,2,4-triazolo containing thiadiazoles (83a-e) and 1,2,4-triazolo-thiadiazole derivatives (84a-d) was evaluated. Compound 84a had good activity toward A. flavus with a MIC value of 70g/mL compared with standard fluconazole; derivatives 83d, 83a,
84c, and 84a demonstrated moderate activity (Figure 64) [147]. The study of the chemical structure of triazole based heterocycles. Bai et al. [148] assessed several novel 1,2,4-triazole analogues for antifungal activity against eight phytopathogens and found that the majority of them exhibited acceptable to outstanding fungicidal characteristics. Almost
all of the compounds demonstrated moderate to excellent fungicidal activity toward the tested phytopathogens. In general, the fungicidal activity of methyl oxime ether group 86 (R1 = benzyl). It is clear that electron-drawing groups at the 2-position of the phenyl ring, such as
85b, 85d, 86b were more helpful for fungicidal activity. Because of the halogen substituent effect, compounds 85b, 85d, 85g, 85k, and 86b demonstrated significantly higher inhibitory activities against fungal pathogens than other compounds, with the chlorine atom playing a more significant role in improving fungicidal activity in each position of the
benzene ring. Furthermore, the prevention rates of compounds 85d, 86e, and 85f against all of the fungi examined were meager. It is shown that for benzyl oxime ether series 85, a bulky 2-tert-butyl group on the benzene substituent was not best for the activity. Compound 85d (2-Cl-4-Br) containing two mixed halogen atoms showed broad-spectrum
fungicidal activity, with EC50 values of 1.59, 0.46, 0.27, and 11.39mg/L against four fungal pathogens (Figure 65). 1,2,4-triazole analogues having a broad spectrum of antifungal activity. The 1,2,4-triazole nucleus and
its derivatives are essential scaffolds in the discovery and development of drugs that have a multitude of biological activities. An acceptable reason for its broad biological profile is a small and stable cyclic ring structure wherein the nitrogen atoms can act both as hydrogen bond donor and as acceptors at the active site of the receptor. The pentacyclic
triazole ring processes plasticity for the synthesis of a number of derivatives due to of its multifold binding sites. This potent scaffold will be a great tool in medicinal chemistry in the future. The most challenging
problem in fungal therapy is antifungal resistance, which may be progressed by drug target overexpression. This review is focused to summarizing recent research on 1,2,4-triazole-hybrids as fungicidal agents over the last decade. It will aid research on 1,2,4-triazole-hybrids as fungicidal agents over the last decade. It will aid research on 1,2,4-triazole-hybrids as fungicidal agents over the last decade.
1,2,4-triazole-moiety. The authors wish to thank the Noncommunicable Diseases Research Center, Fasa University of Medical Sciences. A. flavus: Aspergillus niger. Aspergillus niger. Aspergillus niger. Aspergillus niger. Aspergillus niger. Aspergillus niger.
demethylaseED50:Effective dose for 50% of the populationEWG:Electron withdrawing groupFLC:FluconazoleFO:Fusarium oxysporumK3PO4:Tripotassium phosphateMIC:Minimum inhibitory concentrationNaOH:Sodium hydroxideSAR:Structure-activity relationshipSL:Stemphylium lycopersici.The datasets used and analyzed during the current study
are available from the corresponding author on reasonable request. We have presented all data in the form of figures. This research has been ethically approved (no. 99310) IR.FUMS.REC.1400.013. The authors declare that they have no competing interests. The conception, design, writing, and revision of the study were done by E. Z. The first draft of
the manuscript was written by E. Z., Z. K., M. M., A. S., M. F., and A.K. Also, E. Z. and M. M. played the role of the first author in this manuscript; all authors approved the final manuscript into recent pharmacological advances with structure activity
relationship. European Journal of Medicinal Chemistry. 2018;157:527561. doi: 10.1016/j.ejmech.2018.08.002. [DOI] [PubMed] [Google Scholar]2.Afsarian M. H., Farjam M., Zarenezhad E., Behrouz S., Rad M. N. S. Synthesis, antifungal evaluation and molecular docking studies of some tetrazole derivatives. Acta Chimica Slovenica. 2019;66(4):874887.
doi: 10.17344/acsi.2019.4992. [DOI] [PubMed] [Google Scholar]3.Zarenezhad E., Farjam M., Iraji A. Synthesis and biological activity of pyrimidines-containing hybrids: focusing on pharmacological activity of pyrimidines-containing hybrids: focusing hybrids: focusin
Zarenezhad E., Shams N., Rad M. N. S., Anaraki-Ardakani H., Fayazipoor R. Green synthesis of 5-aryl-(1H,3H,5H,10H)-pyrimido[4,5-b]quinoline-2,4-diones catalysed by 1,4-diazabicyclo[2.2.2]octane in water. Journal of Chemical Research. 2014;38(3):169171. doi: 10.3184/174751914X13917105358323. [DOI] [Google Scholar]5.Dymiska L.
Imidazopyridines as a source of biological activity and their pharmacological potentials-Infrared and Raman spectroscopic evidence of their content in pharmaceuticals and plant materials. Bioorganic & Medicinal Chemistry. 2015;23(18):60876099. doi: 10.1016/j.bmc.2015.07.045. [DOI] [PubMed] [Google Scholar]6.Zarenezhad E., Soltani Rad M. N.
Behrouz S., Esmaielzadeh S., Farjam M. Immobilized [Cu (cdsalMeen)] on silica gel: a highly efficient heterogeneous catalyst for Click[3+2] Huisgen cycloaddition. Journal of the Iranian Chemical Society. 2017;14(2):509519. doi: 10.1007/s13738-016-0999-3. [DOI] [Google Scholar]7.Martnez-Matas N., Rodrguez-Medina J. R. Fundamental concepts of
azole compounds and triazole antifungals: a beginners review. Puerto Rico Health Sciences Journal. 2018;37(3):135142. [PubMed] [Google Scholar]8.Cox J. R., Woodcock S., Hillier I. H., Vincent M. A. Tautomerism of 1,2,3- and 1,2,4-triazole in the gas phase and in aqueous solution: a combined ab initio quantum mechanics and free energy
perturbation study. Journal of Physical Chemistry. 1990;94(14):54995501. doi: 10.1021/j100377a016. [DOI] [Google Scholar]9.Chu X.-M., Wang C., Wang W. L., et al. Triazole derivatives and their antiplasmodial and antimalarial activities. European Journal of Medicinal Chemistry. 2019;166:206223. doi: 10.1016/i.eimech.2019.01.047. [DOI] [PubMed]
[Google Scholar]10.Bekircan O., Mentee E., lker S., Kucuk C. Synthesis of some new 1, 2, 4-triazole derivatives starting from 3-(4-chlorophenyl)-5-(4-methoxybenzyl)-4H-1, 2, 4-triazol with anti-lipase and anti-urease activities. Archiv der Pharmazie. 2014;347(6):387397. doi: 10.1002/ardp.201300344. [DOI] [PubMed] [Google Scholar]11.Cao X., Wang
W., Wang S., Bao L. Asymmetric synthesis of novel triazole derivatives and their in vitro antiviral activity and mechanism of action. European Journal of Medicinal Chemistry. 2017;139:718725. doi: 10.1016/j.ejmech.2017.08.057. [DOI] [PubMed] [Google Scholar]12.Kapro B., Czarnomysy R., Wysokiski M., et al. 1, 2, 4-Triazole-based anticonvulsant
agents with additional ROS scavenging activity are effective in a model of pharmacoresistant epilepsy, Journal of Enzyme Inhibition and Medicinal Chemistry, 2020;35(1):9931002, doi: 10.1080/14756366.2020.1748026, [DOI] [PMC free article] [PubMed] [Google Scholar] [PubMed] [PubM
of 1, 2, 4-triazoles: synthesis, screening & QSAR studies. Current Drug Metabolism. 2014;15(4):389397. doi: 10.2174/1389200215666140908101958. [DOI] [PubMed] [Google Scholar]14. Shafiei M., Peyton L., Hashemzadeh M., Foroumadi A. History of the development of antifungal azoles: A review on structures, SAR, and mechanism of action.
Bioorganic Chemistry. 2020;104:p. 104240. doi: 10.1016/j.bioorg.2020.104240. [DOI] [PubMed] [Google Scholar]15.Russell P. A century of fungicide evolution. The Journal of Agricultural Science. 2005;143(1):1125. doi: 10.1017/S0021859605004971. [DOI] [Google Scholar]16.Pianalto K. M., Alspaugh J. A. New horizons in antifungal therapy. Journal
of Fungi. 2016;2(4):p. 26. doi: 10.3390/jof2040026. [DOI] [PMC free article] [PubMed] [Google Scholar]17.Roemer T., Krysan D. J. Antifungal drug development: challenges, unmet clinical needs, and new approaches. Cold Spring Harbor Perspectives in Medicine. 2014;4(5):p. a019703. doi: 10.1101/cshperspect.a019703. [DOI] [PMC free article]
[PubMed] [Google Scholar]18.Campoy S., Adrio J. L. Antifungals. Biochemical Pharmacology. 2017;133:8696. doi: 10.1016/j.bcp.2016.11.019. [DOI] [PubMed] [Google Scholar]19.Dawson J. H., Sono M. Cytochrome P-450 and chloroperoxidase: thiolate-ligated heme enzymes. Spectroscopic determination of their active-site structures and mechanistic
implications of thiolate ligation. Chemical Reviews. 1987;87(5):12551276. doi: 10.1021/cr00081a015. [DOI] [Google Scholar]20.Kathiravan M. K., Salake A. B., Chothe A. S., et al. The biology and chemistry of antifungal agents: a review. Bioorganic & Medicinal Chemistry. 2012;20(19):56785698. doi: 10.1016/j.bmc.2012.04.045. [DOI] [PubMed]
[Google Scholar]21.Miyamoto Y., Yamazaki C. Synthesis of nitrogen-containing heterocycles. 3. Formation and structure of new 1, 2, 4-triazole derivatives. Journal of Heterocyclic Chemistry. 1989;26(2):327332. doi: 10.1002/jhet.5570260211. [DOI] [Google Scholar]22.Tratrat C. 1, 2, 4-triazole: a privileged scaffold for the development of potent
antifungal agents-a brief review. Current Topics in Medicinal Chemistry. 2020;20(24):22352258. doi: 10.2174/156802662066200704140107. [DOI] [PubMed] [Google Scholar]23.Strzelecka M., witek P. 1, 2, 4-Triazoles as important antibacterial agents. Pharmaceuticals. 2021;14(3):p. 224. doi: 10.3390/ph14030224. [DOI] [PubMed] [Google Scholar]23.Strzelecka M., witek P. 1, 2, 4-Triazoles as important antibacterial agents.
[Google Scholar]24.Samura . Review of antibacterial and antifungal activity of 1, 2, 4-triazole derivatives. Farmatsevtychnyi zhurnal. 2018;5(5):6368. doi: 10.32352/0367-3057.5.15.02. [DOI] [Google Scholar]25.Sahoo S., Veliyath S. K., Mahendra Kumar C. B. Review on substituted 1, 2, 4-triazole as potent antifungal and antibacterial agents.
International Journal of Pharmaceutical Sciences and Research. 2012;3(2012) [Google Scholar]27. Huang T., Jiang H., Zhao Y., He J., Cheng H., Martyniuk C. J. A comprehensive review of 1,2,4-triazole fungicide toxicity in zebrafish (Danio rerio): A mitochondrial and metabolic
perspective. Science of the Total Environment. 2022;809, article 151177 doi: 10.1016/j.scitotenv.2021.151177. [DOI] [PubMed] [Google Scholar]28.Zafar W., Sumrra S. H., Chohan Z. H. A review: pharmacological aspects of metal based 1,2,4-triazole derived Schiff bases. European Journal of Medicinal Chemistry. 2021;222, article 113602 doi:
10.1016/j.ejmech.2021.113602. [DOI] [PubMed] [Google Scholar]29.Blokhina S. V., Sharapova A. V., Ol'khovich M. V., Doroshenko I. A., Levshin I. B., Perlovich G. L. Synthesis and antifungal activity of new hybrids thiazolo[4,5-d]pyrimidines with (1 H-1,2,4)triazole. Bioorganic & Medicinal Chemistry Letters. 2021;40, article 127944 doi:
10.1016/j.bmcl.2021.127944. [DOI] [PubMed] [Google Scholar]30.Aliste M., Prez-Lucas G., Garrido I., Fenoll J., Navarro S. Risk assessment of 1, 2, 4-triazole-typed fungicides for groundwater pollution using leaching potential indices. Water, Air, & Soil Pollution. 2021;232(11):113. doi: 10.1007/s11270-021-05428-1. [DOI] [Google Scholar]31.Bladin J.
A. Ueber von dicyanphenylhydrazin abgeleitete verbindungen. Berichte der deutschen chemischen Gesellschaft. 1885;18(1):4451. [Google Scholar]32.Benson F. R., Savell W. L. The chemistry of the vicinal triazoles. Chemical Reviews. 1950;46(1):168. doi: 10.1021/cr60143a001. [DOI] [PubMed] [Google Scholar]33.Shelke G. M., Rao V., Jha M.,
Cameron T., Kumar A. Microwave-assisted catalyst-free synthesis of substituted 1, 2, 4-triazoles. Synlett. 2015;26(3):404407. doi: 10.1055/s-0034-1379734. [DOI] [Google Scholar]34. Huang H., Guo W., Wu W., Li C. J., Jiang H. Copper-catalyzed oxidative C (sp 3)H functionalization for facile synthesis of 1, 2, 4-triazoles and 1, 3, 5-triazines from
amidines. Organic Letters. 2015;17(12):28942897. doi: 10.1021/acs.orglett.5b00995. [DOI] [PubMed] [Google Scholar]35. Jatangi N., Tumula N., Palakodety R. K., Nakka M. I2-mediated oxidative CN and NS bond formation in water: a metal-free synthesis of 4, 5-disubstituted/n-fused 3-amino-1, 2, 4-triazoles and 3-substituted 5-amino-1, 2, 4-triazoles and 3-substituted/n-fused 3-amino-1, 
thiadiazoles. The Journal of Organic Chemistry. 2018;83(10):57155723. doi: 10.1021/acs.joc.8b00753. [DOI] [PubMed] [Google Scholar]36.Liu J.-Q., Shen X., Wang Y., Wang X. S., Bi X. [3 + 2] cycloaddition of isocyanides with aryl diazonium salts: catalyst-dependent regioselective synthesis of 1,3- and 1,5-Disubstituted 1,2,4-Triazoles. Organic Letters.
2018;20(21):69306933. doi: 10.1021/acs.orglett.8b03069. [DOI] [PubMed] [Google Scholar]37.Chen Z., Li H., Dong W., Miao M., Ren H. I2-catalyzed oxidative coupling reactions of hydrazones and the application in the synthesis of 1, 3, 5-trisubstituted 1, 2, 4-triazoles. Organic Letters. 2016;18(6):13341337. doi:
10.1021/acs.orglett.6b00277. [DOI] [PubMed] [Google Scholar]38.Khan M. A., Polya J. Syntheses of heterocyclic compounds. Part II. N-arylazoles by Ullmann condensation. Journal of the Chemical Society C: Organic. 1970;1(1):8591. doi: 10.1039/j39700000085. [DOI] [Google Scholar]39.Kauffmann T., Legler J., Ludorff E., Fischer H. Synthesis and
```

properties of azole-pyridine combinations: problem of the hydrolytic cleavage of Hetarene combinations. Angewandte Chemie International Edition in English. 1972;11(9):846847. doi: 10.1002/anie.197208461. [DOI] [Google Scholar]40.Olofson R. A., Kendall R. Protection by acylation in the selective alkylation of heterocycles. The Journal of Organic Chemistry. 1970;35(7):22462248. doi: 10.1021/jo00832a031. [DOI] [Google Scholar]41.Ainsworth C., Jones R. Isomeric and nuclear-substituted -Aminoethyl-1, 2, 4-triazoles. Journal of the American Chemical Society. 1955;77(3):621624. doi: 10.1021/jo00832a031.

with phenyllithium in THF ether the position of alkylation is assumed to follow previous examples. Gazzetta Chimica Italiana. 1905;35:p. 373. [Google Scholar]43.Naik A. D., Marchand-Brynaert J., Garcia Y. A simplified approach to N-and N, N-linked 1, 2, 4-triazoles by transamination. Synthesis. 2008;2008(1):149154. doi: 10.1055/s-2007-983896 [DOI] [Google Scholar]44.Wiley R. H., Hart A. J. Reaction of diformylhydrazine with aminoheterocycles. The Journal of Organic Chemistry. 1953;18(10):13681371. doi: 10.1021/jo50016a016. [DOI] [Google Scholar]45.Liu B., Zhang X.-F. The syntheses, structures and fluorescent properties of two 3-D hydrogen- bonded frameworks constructed from monomeric Zn(II) and Cd(II) assemblies containing bitriazole. Inorganic Chemistry Communications. 2007;10(2):199203. doi: 10.1016/j.inoche.2006.10.028. [DOI] [Google Scholar]46.Becker H., Hoffmann G., Gwan K. M., Knpfer L. Azocoupling of quaternary 1, 2, 4-triazolium salts to form 5-p-N, N-dimethylaminophenylazo-1, 2, 4-triazolium salts triazolium salts. Journal fr Praktische Chemie. 1988;330(3):325337. doi: 10.1002/prac.19883300302. [DOI] [Google Scholar]48.Potts K. The chemistry of 1, 2, 4-triazoles. Chemical Reviews. 1961;61(2):87127. doi: 10.1021/cr60210a001. [DOI] [Google Scholar]49.von Meyer W. C., Greenfield S. A., Seidel M. C. Wheat leaf rust: control by 4-n-butyl-1, 2, 4-triazole, a systemic fungicide. Science. 1970;169(3949):997998. doi: 10.1126/science.169.3949.997. [DOI] [PubMed] [Google Scholar]50.Tombo G. M. R., Bellu D. Chirality and crop protection. Angewandte Chemie International Edition in English. 1991;30(10):11931215. doi: 10.1002/anie.199111933. [DOI] [Google Scholar]51.De Beule K., Van Gestel J. Pharmacology of itraconazole. Drugs. 2001;61(Supplement 1):2737. doi: 10.2165/00003495-200161001-00003. [DOI] [PubMed] [Google Scholar]52.Westerberg D. P., Voyack M. J. Onychomycosis: current and the complement of the complement trends in diagnosis and treatment. American Family Physician. 2013;88(11):762770. [PubMed] [Google Scholar]53.Gupta A., Richardson M., Paquet M. Systematic review of oral treatments for seborrheic dermatitis. Journal of the European Academy of Dermatology and Venereology. 2014;28(1):1626. doi: 10.1111/jdv.12197. [DOI] [PubMed] [Google Scholar]53.Gupta A., Richardson M., Paquet M. Systematic review of oral treatments for seborrheic dermatitis. Scholar]54.Rossi S. Australian Medicines Handbook. Adelaide; 2006. [Google Scholar]55.Dayer M. R. Old drugs for newly emerging viral disease, COVID-19: Bioinformatic Prospective. 2020, M. A., Zhu E. S., Thompson G. R., 3rd Isavuconazole in the treatment of invasive aspergillosis and mucormycosis infections. Infection and Drug Resistance. 2016;9:p. 79. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.1093/cid/civ571. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.1093/cid/civ571. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.1093/cid/civ571. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.1093/cid/civ571. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. Clinical Infectious Diseases. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Kauffman C. Isavuconazole: a new broadspectrum triazole antifungal agent. 2015;61(10):15581565. doi: 10.2147/IDR.S81416. [DOI] [PubMed] [Google Scholar]57.Miceli M., Miceli M., Mice Drugs. 2013;73(17):19771983. doi: 10.1007/s40265-013-0152-x. [DOI] [PubMed] [Google Scholar]59.Tschen E. H., Bucko A. D., Oizumi N., Kawabata H., Olin J. T., Pillai R. Efinaconazole solution in the treatment of toenail onychomycosis: a phase 2, multicenter, randomized, double-blind study. Journal of Drugs in Dermatology. 2013;12(2):186192. [PubMed] [Google Scholar]60.Tatsumi Y., Nagashima M., Shibanushi T., et al. Mechanism of action of efinaconazole, a novel triazole antifungal agent. Antimicrobial Agents and Chemotherapy. 2013;57(5):24052409. doi: 10.1128/AAC.02063-12. [DOI] [PMC free article] [PubMed] [Google Scholar]61.Schiller D. S., Fung H. B. Posaconazole: an extended-spectrum triazole antifungal agent. Clinical Therapeutics. 2007;29(9):18621886. doi: 10.1016/j.clinthera.2007.09.015. [DOI] [PubMed] [Google Scholar]62.Rachwalski E. J., Wieczorkiewicz J. T., Scheetz M. H. Posaconazole: an oral triazole with an extended spectrum of activity. Annals of Pharmacotherapy. 2008;42(10):14291438. doi: 10.1345/aph.1L005. [DOI] [PubMed] [Google Scholar]63.Li X., Brown N., Chau A. S., et al. Changes in susceptibility to posaconazole in clinical isolates of Candida albicans. Journal of Antimicrobial Chemotherapy. 2003;53(1):7480. doi: 10.1093/jac/dkh027. [DOI] [PubMed] [Google Scholar]64.Walsh T. J., Raad I., Patterson T. F., et al. Treatment of invasive aspergillosis with posaconazole in patients who are refractory to or intolerant of conventional therapy: an externally controlled trial. Clinical Infectious Diseases. 2007;44(1):212. doi: 10.1086/508774. [DOI] [PubMed] [Google Scholar]65.Raad I. I., Hachem R. Y., Herbrecht R., et al. Posaconazole as salvage treatment for invasive fusariosis in patients with underlying hematologic malignancy and other conditions. Clinical Infectious Diseases. 2006;42(10):13981403. doi: 10.1086/503425. [DOI] [PubMed] [Google Scholar]66.Colon B. L., Rice C. A., Guy R. K., Kyle D. E. Phenotypic screens reveal posaconazole as a rapidly acting amebicidal combination partner for treatment of primary amoebic meningoencephalitis. The Journal of Infectious Diseases. 2019;219(7):10951103. doi: 10.1093/infdis/jiy622. [DOI] [PMC free article] [PubMed] [Google Scholar]67. Vanham D., Spinewine A., Hantson P., Wittebole X., Wouters D., Sneyers B. Drug-drug interactions in the intensive care unit: do they really matter? Journal of Critical Care. 2017;38:97103. doi: 10.1016/j.jcrc.2016.09.014. [DOI] [PubMed] [Google Scholar]68.Patterson T. F., Thompson G. R., III, Denning D. W., et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016;63(4):e1e60. doi: 10.1093/cid/ciw326. [DOI] [PMC free article] [PubMed] [Google Scholar] 69. Omrani A. S., Almaghrabi R. S. Complications of hematopoietic stem transplantation: fungal infections. Hematology/Oncology and Stem Cell Therapy. 2017;10(4):239244. doi: 10.1016/j.hemonc.2017.05.013. [DOI] [PubMed] [Google Scholar] 70. Herbrecht R., Denning D. W., Patterson T. F., et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. New England Journal of Medicine. 2002;347(6):408415. doi: 10.1056/NEJMoa020191. [DOI] [PubMed] [Google Scholar]71.Salvador Velez F. M., Snchez Montalv A., Molina Romero I. Experimental and clinical treatment of Chagas disease: a review. The American Journal of Tropical Medicine and Hygiene. 2017;97(5):12891303. doi: 10.4269/ajtmh.16-0761. [DOI] [PMC free article] [PubMed] [Google Scholar]72.Kumar S., Kimball A. B. New antifungal therapies for the treatment of onychomycosis. Expert Opinion on Investigational Drugs. 2009;18(6):727734. doi: 10.1517/13543780902810352. [DOI] [PubMed] [Google Scholar]72.Kumar S., Kimball A. B. New antifungal therapies for the treatment of onychomycosis. Scholar]73. Pasqualotto A. C., Thiele K. O., Goldani L. Z. Novel triazole antifungal drugs: focus on isavuconazole, ravuconazole, ravuconazole, and albaconazole and albaconazole antifungal activities of posaconazole, ravuconazole, ravuconazole, and voriconazole compared to those of itraconazole and amphotericin B against 239 clinical isolates of Aspergillus spp. and other filamentous fungi: report from SENTRY antimicrobial Agents and Chemotherapy. 2002;46(4):1032-1037.2002. [DOI] [PMC free article] [PubMed] [Google and apphotericin B against 239 clinical isolates of Aspergillus spp. and other filamentous fungi: report from SENTRY antimicrobial Agents and Chemotherapy. Scholar]75.Toribio L., del Nozal M., Bernal J. L., Jimnez J. J., Alonso C. Chiral separation of some triazole pesticides by supercritical fluid chromatography. Journal of Chromatography A. 2004;1046(1-2):249253. doi: 10.1016/S0021-9673(04)01064-7. [DOI] [PubMed] [Google Scholar]76.Sunderland M. R., Cruickshank R. H., Leighs S. J. The efficacy of antifungal azole and antiprotozoal compounds in protection of wool from keratin-digesting insect larvae. Textile Research Journal. 2014;84(9):924931. doi: 10.1177/0040517513515312. [DOI] [Google Scholar]77. Yamaguchi H. Potential of ravuconazole and its prodrugs as the new OralTherapeutics for onychomycosis. Medical Mycology Journal. 2016;57(4):E93E110. doi: 10.3314/mmj.16-00006. [DOI] [PubMed] [Google Scholar]78.Tran N. T., Zivin A., Mozaffarian D., Karmy-Jones R. Right atrial perforation secondary to implantable cardioverter defibrillator insertion. Canadian Respiratory Journal. 2001;8(4) doi: 10.1155/2001/257641. [DOI] [PubMed] [Google Scholar]79.Moberg W. K., Basarab G. S., Cuomo J., Liang P. H. Biologically Active Organosilicon Compounds: Fungicidal Silylmethyltriazoles. ACS; 1987. [DOI] [Google Scholar]80.Bostanian N. J., Larocque N., Chouinard G., Coderre D. Baseline toxicity of several pesticides to Hyaliodes vitripennis (Say)(Hemiptera: Miridae) Pest Management Science: Formerly Pesticides Science. 2001;57(11):10071010. doi: 10.1002/ps.374. [DOI] [PubMed] [Google Scholar]81. Eckert M. R., Rossall S., Selley A., Fitt B. D. L. Effects of fungicides onin vitrospore germination and mycelial growth of the phytopathogensLeptosphaeria maculansandL. biglobosa(phoma stem canker of oilseed rape) Pest Management Science: Formerly Pesticide Science. 2010;66(4):396405. doi: 10.1002/ps.1890. [DOI] [PubMed] [Google Scholar]82.Rani M., Shanker U. Removal of chlorpyrifos, thiamethoxam, and tebuconazole from water using green synthesized metal hexacyanoferrate nanoparticles. Environmental Science and Pollution Research. 2018;25(11):1087810893. doi: 10.1007/s11356-018-1346-2. [DOI] [PubMed] [Google Scholar]83.Wang Z., Tian Z., Chen L., et al. Stereoselective metabolism and potential adverse effects of chiral fungicide triadimenol on Eremias argus. Environmental Science and Pollution Research. 2020;27(8):78237834. doi: 10.1007/s11356-019-07205-4. [DOI] [PubMed] [Google Scholar]84.Krmer W., Schirmer W., U. Modern Crop Protection Compounds. Wiley-VCH; 2007. [Google Scholar]85.Berova M., Zlatev Z. Physiological response and yield of paclobutrazol treated tomato plants (Lycopersicon esculentum Mill.) Plant Growth Regulation. 2000;30(2):117123. doi: 10.1023/A:1006300326975. [DOI] [Google Scholar]86.Schnabel G., Jones A. L. The 14demethylasse(CYP51A1) gene is overexpressed in Venturia inaequalisstrains resistant to myclobutanil. Phytopathology. 2001;91(1):102110. doi: 10.1094/PHYTO.2001.91.1.102. [DOI] [PubMed] [Google Scholar]87. Allen J. W., Wolf D. C. Toxicity profiles in mice treated with hepatotumorigenic and non-hepatotumorigenic triazole conazole fungicides propiconazole, triadimefon, and myclobutanil. Toxicologic Pathology. 2006;34(7):853862. doi: 10.1080/01926230601047816. [DOI] [PubMed] [Google Scholar]88.Ding Z., Ni T., Xie F., et al. Design, synthesis, and structure-activity relationship studies of novel triazole agents with strong antifungal activity against Aspergillus fumigatus. Bioorganic & Medicinal Chemistry Letters. 2020;30(4):p. 126951. doi: 10.1016/j.bmcl.2020.126951. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., Gazzola S., et al. New azole antifungals with a fused triazinone scaffold. European Journal of Medicinal Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., Guillon R., et al. New azole antifungals with a fused triazinone scaffold. European Journal Oliver Alexandria Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020.112082. [DOI] [PubMed] [Google Scholar]89. Montoir D., et al. New azole antifungals with a fused triazinone scaffold. European Journal Oliver Alexandria Chemistry. 2020;189, article 112082 doi: 10.1016/j.ejmech.2020. [DOI] [PubMed] [Google Scholar]89. Montoir D., et al. New azole antifungals with a fused triazinone scaffold. Europ Scholar]90.Xie F., Ni T., Ding Z., et al. Design, synthesis, and _in vitro_ evaluation of novel triazole analogues featuring isoxazole moieties as antifungal agents. Bioorganic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. doi: 10.1016/j.bioorg.2020.103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. [DOI] [PubMed] [Google Scholar]91.Khakzad S., Rahmani F., Hojjati M., Tabandeh M. R. Anti-carcinogenic Chemistry. 2020;101:p. 103982. [DOI] [PubMed] [Pub effects of Satureja khuzistanica and Zataria multiflora essential oils on K562 cell line proliferation. Journal of Food and Bioprocess Engineering. 2019;2(2):127132. [Google Scholar]92.Motahari K., Badali H., Hashemi S. M., et al. Discovery of benzylthio analogs of fluconazole as potent antifungal agents. Future Medicinal Chemistry. 2018;10(9):9871002. doi: 10.4155/fmc-2017-0295. [DOI] [PubMed] [Google Scholar]93. Chandrika N. T., Shrestha S. K., Ngo H. X., Howard K. C., Garneau-Tsodikova S. Novel fluconazole derivatives with promising antifungal activity. Bioorganic & Medicinal Chemistry. 2018;26(3):573580. doi: 10.1016/j.bmc.2017.12.018. [DOI] [PMC free article] [PubMed] [Google Scholar]94.Tekale S., Diwan M. F., Farooqui M., Pardeshi R. K. Design and synthesis of azole containing Imidazole derivatives and evaluation of their antifungal activity. Chemistry & Biology Interface. 2018;8(6) [Google Scholar]95.Wu J., Ni T., Chai X., et al. Molecular docking, design, synthesis and antifungal activity study of novel triazole derivatives. European Journal of Medicinal Chemistry. 2018;143:18401846. doi: 10.1016/j.ejmech.2017.10.081. [DOI] [PubMed] [Google Scholar]96. Sadeghpour H., Khabnadideh S., Zomorodian K., et al. Design, synthesis, and biological activity of new triazole and nitro-triazole derivatives as antifungal agents. Molecules. 2017;22(7):p. 1150. doi: 10.3390/molecules22071150. [DOI] [PMC free article] [PubMed] [Google Scholar]97.Xie F., Ni T., Zhao J., et al. Design, synthesis, and in vitro evaluation of novel antifungal triazoles. Bioorganic & Medicinal Chemistry Letters. 2017;27(10):21712173. doi: 10.1016/j.bmcl.2017.03.062. [DOI] [PubMed] [Google Scholar]98.Chen H.-J., Jiang Y. J., Zhang Y. Q., et al. New triazole derivatives containing substituted 1,2,3-triazole side chains: design, synthesis and antifungal activity. Chinese Chemical Letters. 2017;28(4):913918. doi: 10.1016/j.cclet.2016.11.027. [DOI] [Google Scholar]99.Fang X.-F., Li D., Tangadanchu V. K. R., Gopala L., Gao W. W., Zhou C. H. Novel potentially antifungal hybrids of 5-flucytosine and fluconazole: design, synthesis and bioactive evaluation. Bioorganic & Medicinal Chemistry Letters. 2017;27(22):49644969. doi: 10.1016/j.bmcl.2017.10.020. [DOI] [PubMed] [Google Scholar]100.Xu Y.-Y., Qian A. R., Cao X. F., et al. Design and synthesis of novel triazole derivatives containing -lactam as potential antifungal agents. Chinese Chemical Letters. 2016;27(5):703706. doi: 10.1016/j.cclet.2016.01.040. [DOI] [Google Scholar]101.Zhang Y., Damu G. L. V., Cui S. F., Mi J. L., Tangadanchu V. K. R., Zhou C. H. Discovery of potential antifungal triazoles: design, synthesis, biological evaluation, and preliminary antifungal mechanism exploration. MedChemComm. 2017;8(8):16311639. doi: 10.1039/C7MD00112F. [DOI] [PMC free article] [PubMed] [Google Scholar]103.Mahmoudi Y., Badali H. Hashemi S. M., et al. New potent antifungal triazole alcohols containing N-benzylpiperazine carbodithioate moiety: Synthesis, in vitro evaluation and in silico study. Bioorganic Chemistry. 2019;90, article 103060 doi: 10.1016/j.bioorg.2019.103060. [DOI] [PubMed] [Google Scholar]104.Li B., Zhang D., Zhang Y., et al. Synthesis and evaluation of novel benzene-ethanol bearing 1, 2, 4-triazole derivatives as potential antimicrobial agents. Medicinal Chemistry Research. 2017;26(1):4451. doi: 10.1007/s00044-016-1724-6. [DOI] [Google Scholar]105. Hoshi T., Yamada K., Yoshizawa Y., Oh K. Structure-activity relationship study for fungicidal activity of 1-(4-phenoxymethyl-2-phenyl-[1, 3] dioxolan-2ylmethyl)-1H-1, 2, 4-triazole derivatives against rice blast. Journal of Plant Protection Research. 2015;55(4):383388. doi: 10.1515/jppr-2015-0051. [DOI] [Google Scholar]106.Al-Wabli R. I., Alsulami M. A., Bukhari S. I., Moubayed N., Al-Mutairi M. S., Attia M. I. Design, synthesis, and antimicrobial activity of certain new Indole-1, 2, 4 Triazole conjugates. Molecules. 2021;26(8):p. 2292. doi: 10.3390/molecules26082292. [DOI] [PMC free article] [PubMed] [Google Scholar]107.Zhao X., Liao A., Zhang F., et al. Design, synthesis, and bioactivity of nortopsentin analogues containing 1,2,4triazole moieties. Journal of Heterocyclic Chemistry. 2020;57(2):761767. doi: 10.1002/jhet.3817. [DOI] [Google Scholar]108.Ahuja R., Sidhu A., Bala A., Arora D., Sharma P. Structure based approach for twin-enzyme targeted benzimidazolyl-1,2,4-triazole molecular hybrids as antifungal agents. Arabian Journal of Chemistry. 2020;13(6):58325848. doi: 10.1016/j.arabjc.2020.04.020. [DOI] [Google Scholar]109.Karaca Gener H., Acar evik U., Levent S., et al. New benzimidazole-1, 2, 4-triazole hybrid compounds: synthesis, anticandidal activity evaluation. Molecules 2040507. [DOI] [PMC free article] [PubMed] [Google Scholar]110.Can N.., Acar evik U., Salk B. N., et al. Synthesis, molecules 2040507. [DOI] [PMC free article] (PubMed] [Google Scholar]110.Can N.., acar evik U., Salk B. N., et al. Synthesis, anticandidal activity evaluation of new benzimidazole-triazoles as potential lanosterol 14-demethylase inhibitors. Journal of Chemistry. 2017;2017:15. doi: 10.1155/2017/9387102. [DOI] [Google Scholar]111. Jiang L., Wang M. Y., Wan F. X., Qu Z. Q. Synthesis and biological activity of tri-substituted 1, 2, 4-triazoles bearing benzimidazole moiety. Phosphorus, Sulfur, and Silicon and the Related Elements. 2015;190(10):15991605. [Google Scholar]112.Luo Y.-L., Baathulaa K., Kannekanti V. K., Zhou C. H., Cai G. X. Novel benzimidazole derived naphthalimide triazoles: synthesis, antimicrobial activity and interactions with calf thymus DNA. Science China Chemistry. 2015;58(3):483494. doi: 10.1007/s11426-014-5296-3. [DOI] [Google Scholar]112.Luo Y.-L., Baathulaa K., Kannekanti V. K., Zhou C. H., Cai G. X. Novel benzimidazole derived naphthalimide triazoles: synthesis, antimicrobial activity and interactions with calf thymus DNA. Science China Chemistry. 2015;58(3):483494. doi: 10.1007/s11426-014-5296-3. [DOI] [Google Scholar] [Google Scholar] [DOI] [Google Scholar] Scholar]113.Somagond S. M., Kamble R. R., Kattimani P. P., Joshi S. D., Dixit S. R. Design, synthesis, docking and in vitro antifungal study of 1, 2, 4-triazole hybrids of 2-(aryloxy) quinolines. Heterocyclic Communications. 2017;23(4):317324. [Google Scholar]114.DSouza V. T., Nayak J., DMello D. E., Dayananda P. Synthesis and characterization of biologically important quinoline incorporated triazole derivatives. Journal of Molecular Structure. 2021;1229:p. 129503. doi: 10.1016/j.molstruc.2020.129503. [DOI] [Google Scholar]115.Fan Z., Shi J., Luo N., Ding M., Bao X. Synthesis, crystal structure, and agricultural antimicrobial evaluation of novel quinazoline thioether derivatives incorporating the 1, 2, 4-triazolo [4, 3-a] pyridine moiety. Journal of Agricultural and Food Chemistry. 2019;67(42):1159811606. doi: 10.1021/acs.jafc.9b04733. [DOI] [PubMed] [Google Scholar]116.Fan Z., Shi J., Luo N., Bao X. Synthesis, crystal structure and antimicrobial activity of 2-((2-(4-(1H-1,2,4-triazol-1-yl)phenyl)quinazolin-4-yl)oxy)-N-phenylacetamide derivatives against phytopathogens. Molecular Diversity. 2019;23(3):615624. doi: 10.1007/s11030-018-9896-2. [DOI] [PubMed] [Google Scholar]117. Abuelizz H. A., el-Dib R. A., Marzouk M., al-Salahi R. In vitro evaluation of new 2-phenoxy-benzo[g][1,2,4]triazolo[1,5-a]quinazoline derivatives as antimicrobial agents. Microbial Pathogenesis 2018;117:6067. doi: 10.1016/j.micpath.2018.02.018. [DOI] [PubMed] [Google Scholar]118.El-Attar Z. Synthesis of pyrazolo-1, 2, 4-triazolo [4, 3-a] quinoxalines as antimicrobial agents with potential inhibition of DHPS enzyme. Future Medicinal Chemistry. 2018;10(18):21552175. doi: 10.4155/fmc-2018-0082. [DOI] [PubMed] [Google Scholar]119.Yang L., Bao X.-P. Synthesis of novel 1, 2, 4-triazole derivatives containing the quinazolinylpiperidinyl moiety and N-(substituted phenyl) acetamide group as efficient bactericides against the phytopathogenic bacterium Xanthomonas oryzae pv. oryzae. RSC Advances. 2017;7(54):3400534011. doi: 10.1039/C7RA04819J. [DOI] [Google Scholar]120.Sompalle R., Roopan S. M., al-Dhabi N. A., Suthindhiran K., Sarkar G., Arasu M. V. 1,2,4-Triazolo-quinazoline-thiones: non-conventional synthetic approach, study of solvatochromism and antioxidant assessment. Journal of Photochemistry and Photobiology B: Biology. 2016;162:232239. doi: 10.1016/j.jphotobiol.2016.06.051. [DOI] [PubMed] [Google Scholar]121.Khan G., Sreenivasa S., Govindaiah S., Chandramohan V., Shetty P R. Synthesis, biological screening, in silico study and fingerprint applications of novel 1, 2, 4-triazole derivatives. Journal of Heterocyclic Chemistry. 2020;57(4):20102023. doi: 10.1002/jhet.3929. [DOI] [Google Scholar]122.Jin R., Wang Y., Guo H., et al. Design, synthesis biological activity, crystal structure and theoretical calculations of novel 1,2,4-triazole derivatives. Journal of Molecular Structure. 2020;1202, article 127234 doi: 10.1016/j.molstruc.2019.127234. [DOI] [Google Scholar]123.Wu W.-N., Jiang Y. M., Fei Q., du H. T. Synthesis and fungicidal activity of novel 1, 2, 4-triazole derivatives containing a pyrimidine moietv. Phosphorus, Sulfur, and Silicon and the Related Elements. 2019;194(12):11711175. doi: 10.1080/10426507.2019.1633321. [DOI] [Google Scholar]124.Patel D. M., Vala R. M., Sharma M. G., Rajani D. P., Patel H. M. A practical green visit to the functionalized [1, 2, 4] triazolo [5, 1-b] quinazolin-8 (4H) one scaffolds using the group of the group of the process of the functionalized [1, 2, 4] triazolo [5, 1-b] quinazolin-8 (4H) one scaffolds using the group of the grou assisted purification (GAP) chemistry and their pharmacological testing. Chemistry Select. 2019;4(3):10311041. [Google Scholar]125.Beyzaei H., Khosravi Z., Aryan R., Ghasemi B. A green one-pot synthesis of 3 (5)-substituted 1, 2, 4-triazol-5 (3)-amines as potential antimicrobial agents. Journal of the Iranian Chemical Society. 2019;16(12):25652573 doi: 10.1007/s13738-019-01714-2. [DOI] [Google Scholar]126.Appna N. R., Nagiri R. K., Korupolu R. B., et al. Design and synthesis of novel 4-hydrazone functionalized/1, 2, 4-triazole fused pyrido [2, 3-d] pyrimidine derivatives, their evaluation for antifungal activity and docking studies. Medicinal Chemistry Research. 2019;28(9):15091528. doi: 10.1007/s00044-019-02390-w. [DOI] [Google Scholar]127.Singh R., Kashaw S. K., Mishra V. K., Mishra V [Google Scholar]128.Jin R.-Y., Zeng C. Y., Liang X. H., et al. Design, synthesis, biological activities and DFT calculation of novel 1,2,4-triazole Schiff base derivatives. Bioorganic Chemistry. 2018;80:253260. doi: 10.1016/j.bioorg.2018.06.030. [DOI] [PubMed] [Google Scholar]129.Zhang Y., Zhan Y. Z., Ma Y., et al. Synthesis, crystal structure and 3D-QSAR studies of antifungal (bis-)1,2,4-triazole Mannich bases containing furyl and substituted piperazine moieties. Chinese Chemical Letters. 2018;29(3):441446. doi: 10.1016/j.cclet.2017.08.035. [DOI] [Google Scholar]130.Sui G., Zhang W., Zhou K., et al. Trialkylamine derivatives containing a triazole moiety as promising ergosterol biosynthesis inhibitor: design, synthesis, and antifungal activity, Chemical and Pharmaceutical Bulletin. 2017;65(1):8289. doi: 10.1248/cpb.c16-00732. [DOI] [PubMed] [Google Scholar]131.Mu J.-X., Shi Y. X., Wu H. K., et al. Microwave assisted synthesis, antifungal activity, DFT and SAR study of 1, 2, 4-triazolo [4, 3-a] pyridine derivatives containing hydrazone moieties. Chemistry Central Journal. 2016;10(1):19. doi: 10.1186/s13065-016-0196-6. [DOI] [PMC free article] [PubMed] [Google Scholar]132.Zoidis G., Kritsi E., Lecinska P., et al. The triazole ring as a privileged scaffold for putative antifungals: synthesis and evaluation of a series of new analogues. ChemMedChem. 2021;16(1):134144. doi: 10.1002/cmdc.202000312. [DOI] [PubMed] [Google Scholar]133.Dincel E. D., Ulusoy-Gzeldemirci N., atana D., Kkbasmac . Design, synthesis, characterization and antimicrobial evaluation of some novel hydrazinecarbothioamide, 4-thiazolidinone and 1,2,4triazole3thione derivatives. Journal of Heterocyclic Chemistry. 2021;58(1):195205. doi: 10.1002/jhet.4159. [DOI] [Google Scholar]134.Cheng Y.-N., Jiang Z. H., Sun L. S., Su Z. Y., Zhang M. M., Li H. L. Synthesis of 1, 2, 4-triazole benzoyl arylamine derivatives and their high antifungal activities. European Journal of Medicinal Chemistry. 2020;200:p. 112463. doi: 10.1016/j.ejmech.2020.112463. [DOI] [PubMed] [Google Scholar]135.Stingaci E., Zveaghinteva M., Pogrebnoi S., et al. New vinyl-1,2,4-triazole derivatives as antimicrobial agents: Synthesis, biological evaluation and molecular docking studies. Bioorganic & Medicinal Chemistry Letters. 2020;30(17, article 127368) doi: 10.1016/j.bmcl.2020.127368. [DOI] [PubMed] [Google Scholar]136.Wu W. N., Jiang Y. M., Fei Q., du H. T., Yang M. F. Synthesis and antifungal activity of novel 1,2,4triazole derivatives containing an amide moiety. Journal of Heterocyclic Chemistry. 2020;57(3):13791386. doi: 10.1002/jhet.3874. [DOI] [Google Scholar]137.Yurtta L., Cantrk Z. The synthesis, antifungal and apoptotic effects of triazole-oxadiazoles against Candida species. European Journal of Medicinal Chemistry. 2018;144:255261. doi: 10.1016/j.ejmech.2017.12.020. [DOI] [PubMed] [Google Scholar]138.Li B., Lin X., Zhang Y., Zhang Y., Zhang D., Xiao Y., Lin F. Synthesis and characterization of novel N-phenylacetamide bearing 1, 2, 4-triazole derivatives as potential antimicrobial agents. Chemical Research in Chinese Universities. 2017;33(1):7073. doi: 10.1007/s40242-017-6327-3. [DOI] [Google Scholar]139.Pricopie A.-I., Vlase L., Prnu A., Cristian D. Design and synthesis of some novel 1, 2, 4-triazole-3-yl-mercapto derivatives as potential anti-Candida agents. Enzyme. 2018;66(6):948958. doi: 10.31925/farmacia.2018.6.4. [DOI] [Google Scholar]140.Lin G.-S., Duar W. G., Yang L. X., Huang M., Lei F. H. Synthesis and antifungal activity of novel myrtenal-based 4-methyl-1, 2, 4-triazole-thioethers. Molecules 2020193. [DOI] [PMC free article] [PubMed] [Google Scholar]141. Cheng D., Wei W., Li Y., et al. Design, synthesis and biological activities of novel 4, 5-disubstituted-3-S-(-D-acetylglycosyl)-1, 2, 4-triazole derivatives. Chemical Research in Chinese Universities. 2017;33(5):758764. doi: 10.1007/s40242-017-7053-6. [DOI] [Google Scholar]142.Bitla S., Gayatri A. A., Puchakayala M. R., et al. Design and synthesis, biological evaluation of bis-(1,2,3- and 1,2,4)-triazole derivatives as potential antimicrobial and antifungal agents. Bioorganic & Medicinal Chemistry Letters. 2021;41, article 128004 doi: 10.1016/j.bmcl.2021.128004. [DOI] [PubMed] [Google Scholar]143.Beyzaei H., Ghanbari Kudeyani M., Samareh Delarami H., Aryan R. Synthesis, antimicrobial and antioxidant evaluation, and molecular docking study of 4,5-disubstituted 1,2,4-triazole-3-thiones. Journal of Molecular Structure. 2020;1215, article 128273 doi: 10.1016/j.molstruc.2020.128273. [DOI] [Google Scholar]144.Galstyan A. S., Ghochikyan T. V., Samvelyan M. A., Frangyan V. R., Sarfraz M. Synthesis, study of the biological activity in a series of the latter. ChemistrySelect. 2019;4(42):1238612390. doi: 10.1002/slct.201902761. [DOI] [Google Scholar]145.Sidhu A., Kukreja S. Synthesis of novel fluorinated benzothiazol-2-yl-1,2,4-triazoles: Molecular docking, antifungal evaluation and in silico evaluation for SAR. Arabian Journal of Chemistry. 2019;12(8):21182127. doi: 10.1016/j.arabjc.2015.01.009. [DOI] [Google Scholar]146.Shingare R. M., Patil Y. S., Sangshetti J. N., Damale M. G., Rajani D. P., Madje B. R. Synthesis, antimicrobial evaluation and docking study of some pyrazole bearing [1, 2, 4] triazolo [3, 4-b][1, 3, 4] thiadiazole derivatives. ChemistrySelect. 2018;3(14):38993903. doi: 10.1002/slct.201800373 [DOI] [Google Scholar]147.Sahi S., Sodhi R. K., Jamwal B., Paul S. Synthesis and in vitrobiological evaluation of some novel triazole-based heterocycles as potential antimicrobial agents. Journal of Heterocycles as po Design, synthesis and fungicidal activity of new 1, 2, 4-triazole derivatives containing oxime ether and phenoxyl pyridinyl moiety. Molecules 25245852. [DOI] [PMC free article] [PubMed] [Google Scholar]This section collects any data citations, data availability statements, or supplementary materials materials (pubMed) [Google Scholar]This section collects any data citations, data availability statements, or supplementary materials (pubMed) [Google Scholar]This section collects any data citations (pubmed) [Doogle Scholar]This section collects (pubmed) [Doogle Scholar]This section col included in this article. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request. We have presented all data in the form of figures. Articles from BioMed Research International are provided here courtesy of Wiley Antifungal triazole agents (fluconazole, voriconazole, itraconazole and posaconazole) are widely used for the management of invasive fungal infections (IFI). These drugs are indicated both for the prophylaxis and treatment of IFI, particularly in candidiasis and aspergillosis, major cause of mortality in immunocompromised patients. Due to a large interindividual pharmacokinetic variability leading to sub-therapeutic or toxic concentrations and to concentration-efficacy and/or -toxicity relationships, therapeutic drug monitoring (TDM) of antifungal triazole is fully justified. This review provides an overview of literature based data that confirm the usefulness of such TDM and its level of evidence as well as the practical guidelines for its implementation. In addition, we discuss the interest of new tools to improve the clinical management of IFI, such as genotyping tests optimizing initial voriconazole dosing regimen or the development of a new solid oral tablet of posaconazole improving its bioavailability and limiting absorption disorders. Keywords: interindividual variability; pharmacokinetic; therapeutic drug monitoring; triazole antifungal.

Triazole antifungal side effects. Triazole antifungal examples. Triazole medication. What are triazole antifungals. Triazole fungicide.