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ROLE OF AZOLE ANTIFUNGAL AGENTS IN SEBORRHEIC DERMATITIS & DANDRUFF: A REVIEW

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ABSTRACT

Seborrheic Dermatitis (SD) also known as Dandruff which affects the Seborrheic area of the body (Skin and cavities). In this review, summarize the current knowledge including chemistry, pathophysiology, and treatment with azole antifungal agents. Azole antifungal agents are currently used in various fungal infections mainly as topical preparation such as cream, ointment, shampoo, gel, etc. most clinically useful drugs are Ketoconazole, Miconazole, Metronidazole, Itraconazole, Bifonazole Most imidazole derivatives are suitable for topically used because of their poor absorption and tolerable in systemically (Clotrimazole, Oxiconazole, Econazole, Isoconazole, Bifonazole, etc.). Miconazole can be given systemically or locally, Ketoconazole orally active because of better absorption Fluconazole and Itraconazole are newer orally effective triazole derivatives. Imidazole derivatives act as fungistatic (stop fungal growth) or fungicidal (destroy the fungus), they act by inhibiting sterol (ergosterol) synthesis, as it is an integral part of the cytoplasmic cell membrane of fungi.

KEYWORDS: Azole, Dandruff, Imidazole Antifungal drugs, Seborrheic Dermatitis.

INTRODUCTION

Seborrheic Dermatitis (SD) are chronic, long-lasting, dermatologic inflammatory state they affect have high lipid consuming body part like eyebrow (Figure 1), chest (Figure 2), ear (Figure 3), hair (Figure 4), and nose (Figure 5). Seborrheic Dermatitis prevalence in humans is approximately 1-3% in normal citizens and in immunodeficient humans approximately have 34 -83%.[1,2,3] that highly affect the winter they influence by UV light that elaborate. That enhances the clinical appearance by exposing it to sunlight have some corroboration.[4] their diagnosis of SD based on the which part of body effect is white and yellow greasy

material in the surface of scalp in teenage and younger SD are oily and peeling off the surface of the scalp and redness on skin their correct diagnosis in through distribution of lesions and affected area of their body.[7] Mainly used treatment of SD based on the quantity of grain (peeling) and how much affect the infected area on the basis of using treatment.[8] these fungi utilize oil on the skin exterior create unsaturated or saturated fats and affect the surface of the skin and create inflammation effect .there sebaceous gland secretes oily and waxy matter induce the cultivation of *P. ovale* these produces SD there using antifungal medication SD have caused by Malassezia Yeasts but in which have some controversy.[9]

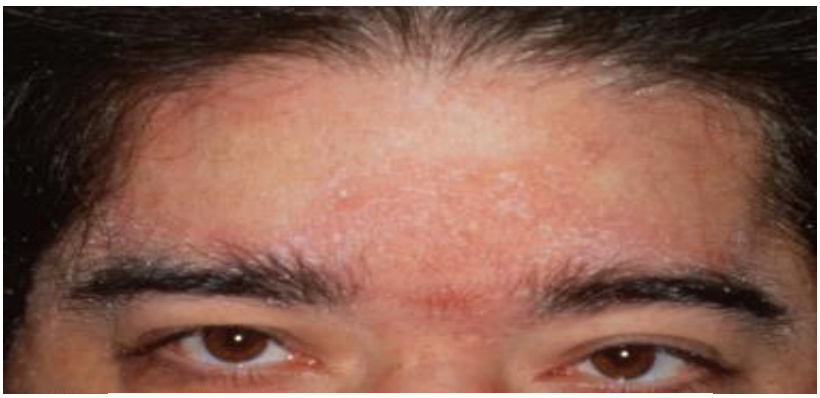


Figure 1: Seborrheic dermatitis on eyebrow.

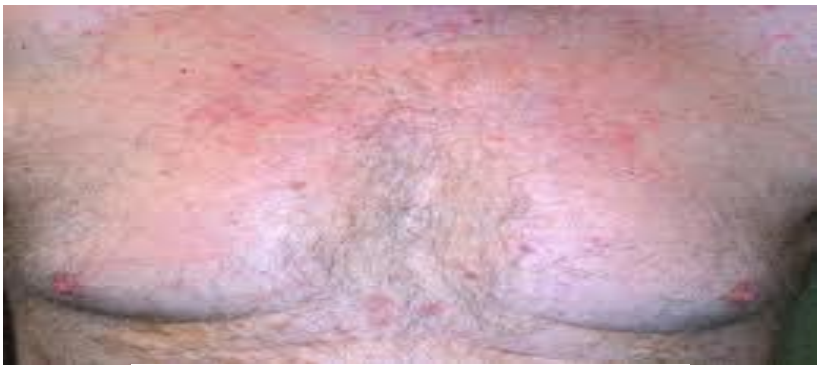


Figure 2: Seborrheic dermatitis on chest.

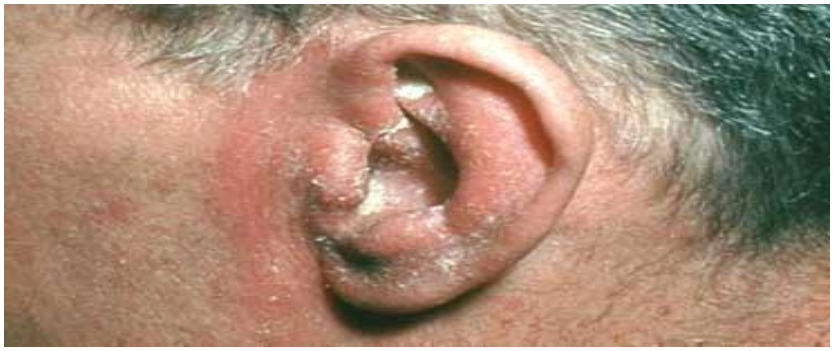


Figure 3: Seborrheic dermatitis on ear.

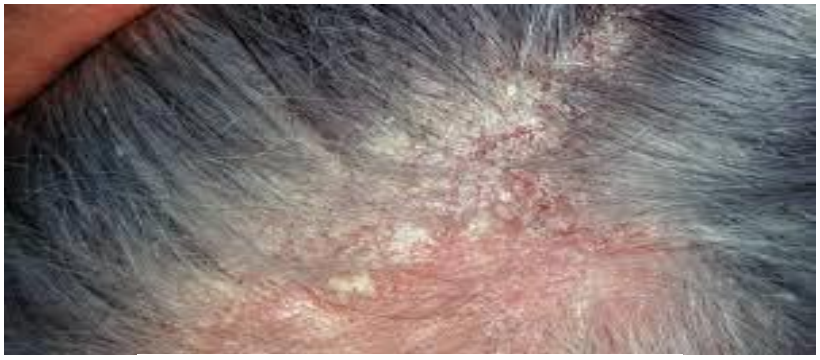


Figure 4: Seborrheic dermatitis on hair.

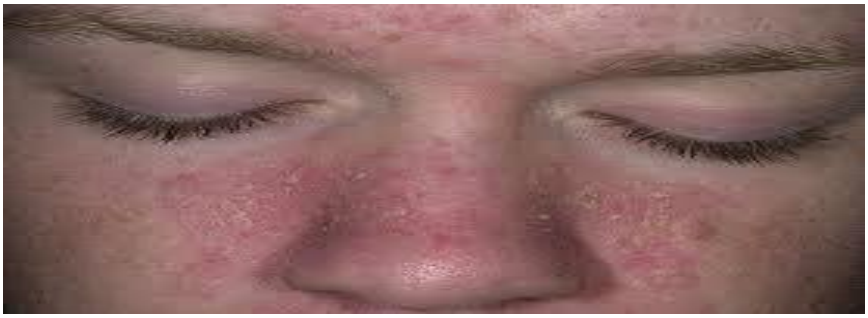


Figure 5: Seborrheic dermatitis on nasal folds.

Malassezia yeasts: Malassezia yeast genus Malassezia is obtained in the human skin and they are lipotropic in nature and there are two species, *P. ovale* and *P. orbiculare* on the cause of cell morphology (Gueho *et al.*1996).[5] Malassezia yeasts produce disorder, their connection linking SD and yeast there various argument, *P. ovale* is the etiologic substance of SD their various research have treatment of SD using antifungal like azole derivative orally and topically and improve their immune system through antimicrobial antibiotics.[6]

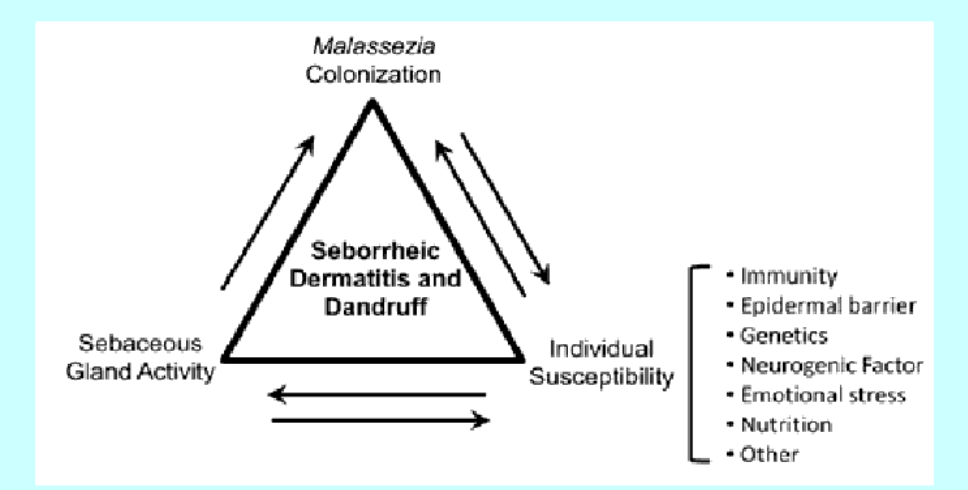


Figure 6: Predisposing factor interaction in the pathogenesis seborrheic Dermatitis & Dandruff treatment.

The primary treatment of the SD using moisturizer for moist and lose flakes like petroleum jelly and mineral oil there flakes pill to by hairbrush and warm water absorb by cloth and scrub it, these are primary treatment and there apply ketoconazole 1% and 2% cream and foam based apply twice a day for two weeks.[10] US FOOD DRUG ADMINISTRATION not approved shampoo for the treatment of SD on younger children (2 years) and there are various azole derivatives used in the treatment of SD and dandruff.

Role of azole

Mostly antifungal drugs have azole derivatives are the biggest class of antifungal drugs used for the treatment of Seborrheic dermatitis and dandruff these are used both orally and topically used these are divided into two categories on structural based, first one Imidazoles (Clotrimazole, miconazole, ketoconazole) there have 2 nitrogen group and five membrane ring, the second one are triazole (fluconazole, Voriconazole, itraconazole) there have three mitogens with five membrane ring.[11] Azoles are the inhibition of the growth of a wide range of fungus by inhibiting the cytochrome P450 depends on the enzyme lanosterol 14α-demethylase that is responsible for the conversion of lanosterol to ergosterol that inhibits the important item of the cell.[12]

Topical azole antifungal agents

Class	Antifungal Agent	Formulations Available	Mode of Application	Mechanism of Action
Azoles	Ketoconazole	2% Shampoo, 2% Cream	Shampoo: 1-3 times per week for 4-8 Weeks. Cream: Twice a day	Inhibition of fungal lanosterol 14-α demethylase enzyme resulting in depletion of ergosterol and accumulation of toxic sterols in fungal cell membrane
	Fluconazole	2% Shampoo, 0.5% Gel	Shampoo: 2-3 times per week for 4 weeks Gel: 1-2 times daily	
	Clotrimazole	1% Cream, Lotion	Twice daily	
	Sertaconazole	2% Cream, Lotion	Twice daily	
	Micnoazole	2% Cream, Gel	Twice daily	
	Oxiconazole	1% Cream, Lotion	Once daily	
	Bifonazole	1% Cream, Shampoo	Once daily	
	Flutrimazole	1% Shampoo, 1% Gel	Shampoo: 1-2 times per week for 4 weeks Gel: Once daily	
	Climbazole	1% lotion, 0.5% Shampoo	Lotion:overnight applicationShampoo:2times per week for 4 weeks	

Ketoconazole: Ketoconazole is an imidazole subordinate initially endorsed by the FDA in 1981. It is accessible in 1% and 2% cleanser and cream formulations.[13] In 2007, ketoconazole froth, 2%, was endorsed in the United States for the topical treatment of SD when utilized twice day by day for about a month in patients 12 years and older.[14] There are reports of better viability of 2% plans when contrasted with the ones with 1% ketoconazole.[15] Absorption of ketoconazole through the skin is immaterial, with no ketoconazole identified in plasma after topical utilization of ketoconazole cream or shampooing. Around 5% of the medication is found to enter into the hair keratin 12 hours after a solitary cleanser. It is named a pregnancy classification C drug. Various investigations led on ketoconazole have utilized it in fluctuating dosages. The most successive portion was 2% twice day by day consistently over face and 2% two times every week over the scalp.[16]

Fluconazole: Fluconazole, an individual from the triazole antifungal family, was endorsed by perspiration and diffuses quickly and widely in the layer corneum. Its focus in the skin is higher than in the serum. The drawn-out skin maintenance of fluconazole (7 days subsequent to halting treatment) has been credited to its high liking to layer corneum because of communication between fluconazole and keratin.[17] However, skin dispersion after the topical organization has not been concentrated widely. Despite the fact that facial SD has been accounted for to react to fluconazole 2% cleanser in a study, there is an absence of studies in the writing examining the utilization of topical fluconazole in SD.[18]

Clotrimazole: Clotrimazole is a wide range antifungal operator of the imidazole family. Topical Clotrimazole is named a pregnancy classification B sedate. When all is said in done, it is very much endured by most patients. Incidentally, patients may encounter bothering with a consuming sensation at the site of utilization. Unfavorably susceptible contact dermatitis with erythema, edema, urticaria, and pruritus has been accounted for rarely. However, there is a lack of studies in the writing on utilization of this medication in SD.

Sertaconazole: It is additionally an expansive range antifungal operator of the imidazole family. It is accessible in cream, salve, and cleanser details. Topical Sertaconazole is named a pregnancy class C drug. It is likewise all around endured when applied topically with infrequent nearby site aggravation/consuming sensation. The special benzothiophene ring in the synthetic structure offers higher lipophilicity and more prominent maintenance of medication in the layer corneum) for as long as 48 hours, prompts more prominent mycological fix rates and lesser possibility of relapse.[20] Treatment with Sertaconazole

likewise brings about the enlistment of cyclooxygenase-2 (COX-2) and the ensuing arrival of prostaglandin E2 (PGE2), in this manner giving calming restorative benefits.[21] It is generally all-around endured, anyway infrequently barely any reactions like pruritus, contact dermatitis, consuming sensation, application site erythema has been noted.[19]

An examination was embraced to think about the adequacy of Sertaconazole 2% cream versus Clotrimazole 1% cream for the treatment of SD of the face. 128 patients were encouraged to utilize these creams twice day by day for about a month. The deliberate result quiet fulfillment rates were higher in the Sertaconazole group.[22] Another examination demonstrated that topical Sertaconazole is similarly powerful at clearing SD as tacrolimus 0.03% topical preparation.[23] In an investigation directed by Lotti *et al*. 24 in 132 patients of SD, the gathering of patients getting Sertaconazole 2% cream indicated improvement practically identical with the gathering accepting ketoconazole 2% cream.[24]

Miconazole: Micnoazole is accessible in 2% cream, 2% gel, and cleanser definitions. It is a pregnancy class B medication. It has a great entrance in layer corneum following topical application to skin.10 a randomized, twofold visually impaired, relative, equal gathering, a multicenter study directed in Switzerland indicated that miconazole cleanser, when utilized two times per week is at any rate as viable and protected as ketoconazole cleanser in treating scalp SD. Another randomized, twofold visually impaired, relative, equal gathering, multicenter study was done on 274 patients (145 miconazole, 129 ketoconazole). Treatment was twice-week by week for about a month. Evaluations included side effects of erythema, tingling, scaling ['Symptom Scale of Seborrhoeic Dermatitis' (SSSD)], infection seriousness, and worldwide change [Clinical Global Impressions (CGIs) and Patient Global Impressions (PGIs)]. They reasoned that miconazole is at any rate as compelling and sheltered as ketoconazole in treating scalp SD.[25]

Bifonazole: Bifonazole is a subbed imidazole antifungal specialist which has an expansive range of movement in vitro against dermatophytes, molds, yeasts, dimorphic parasites, and some Gram-positive microbes. It is accessible in 1% cream and cleanser arrangements. Contrasted and most of the topical antifungal medications, which should be applied in any event twice day by day, bifonazole offers the accommodation of once day by day organization, which may improve tolerant compliance.[26] In a randomized report led by Zienicke *et al*. 100 patients were enlisted and treated with either bifonazole 1% cream or the relating vehicle once day by day for about a month. All patients were likewise assessed

following a month and a half of development. Clinical assessment depended on the accompanying parameters: erythema, papules, invasion, scaling, and tingle. What's more, the mycological assessment was performed utilizing satisfactory contact plates for quantitative assurance of *Malassezia furfur*. There was a measurably noteworthy improvement in every one of these parameters in the patient gathering that applied bifonazole.[27] In another examination directed more than twenty-five patients with SD confined to the face, bifonazole cream was applied once a day by day, and 21 (84%) patients were liberated from sores toward the finish of about a month. It has likewise been accounted for to have a calming action.[28]

Flutrimazole: Flutrimazole is another imidazole antifungal specialist whose antifungal action against *Malassezia furfur spp* in guinea pigs in vivo has been demonstrated to be better than sertaconazole, however lower than ketoconazole and bifonazole.[29] In an investigation directed by Noguera *et al.*[30] it was reasoned that Flutrimazole gel 1% has comparative adequacy to ketoconazole gel at a portion of three applications for every week for 28 days.

Climbazole: Pople *et al*. observed that Climbazole application to scalp results in an up-regulation in expression of a number of genes including those encoding proteins involved in cornified envelope formation and further studies demonstrated that this does translate into increased protein expression. These studies suggest Climbazole, besides its antifungal activity, is delivering positive skin benefits helping to relieve dandruff symptoms effectively.[31] A double-blind, comparative, prospective, longitudinal study was conducted on 60 patients of scalp SD for six weeks. Patients were assigned randomly to one of two treatment groups 1% ketoconazole shampoo and 1% Climbazole shampoo for once-daily application. After six weeks, the results showed that both drugs were effective in treating symptoms of itching, peeling, dry or oily skin, but 1% ketoconazole shampoo showed superior efficacy, with a statistically significant difference in all symptoms. 80% of patients in the ketoconazole group and 13% of the Climbazole group were observed to achieve clinical cure at end of treatment ($p = 0.0001$).[32]

Pharmacology of azoles

Regardless of contrasts in the organization of the cell membrane and the nearness of the cell wall, parasites are metabolically like mammalian cells and offer barely any pathogen-explicit targets. Foundational antifungal specialists can be commonly assembled based on their site of activity in pathogenic organisms. Azole antifungal operators apply their antifungal impacts

by focusing on ergosterol—the foremost cell film sterol of numerous pathogenic organisms. By restraining *14α-demethylase* (*lanosterol demethylase*), a contagious cytochrome P450 (CYP)– subordinate catalyst, azole antifungal specialists drain cell layer ergosterol, disable film ease, and lead to the gathering of harmful 14α-methylated sterols, bringing about development capture and inevitable parasitic cell death.[33] However, this hindrance is not completely particular to growths; to be sure, insurance restraint of human CYP compounds by azoles is frequently liable for pharmacokinetic tranquilize sedate connections. The parasitic objective for azole restricting is heme-containing pockets on the *14α-demethylase* enzyme.[34] Differences in the compliance of the *14α-demethylase* restricting pocket and azole structure to a great extent characterize the coupling fondness of each medication, and in some contagious species, the potential for cross-opposition among triazoles.[34]

For particles got from ketoconazole (example: Itraconazole, Posaconazole), augmentation of the nonpolar side chains improves azole official to the *14α-demethylase* Apo protein, bringing about an upgraded range of movement against molds. Voriconazole, a subsidiary of fluconazole, has a α-o-methyl bunch that gives action against *Aspergillus species* and different filamentous fungi. Resistance to triazole antifungal specialists is most regularly the after effect of transformations in the azole restricting pocket of *14α-demethylase*[35,36] and additionally the overexpression of MDR1 efflux siphons that remove fluconazole or the multidrug adenosine triphosphate–subordinate efflux siphons CDR1 and CDR2, which oust all triazoles, in this way prompting cross-resistance. Because inherent obstruction in *C krusei* is a consequence of impeded authority of fluconazole to *14α-demethylase*, more up-to-date triazoles with an improved official to the protein hold action against fluconazole-safe strains, for example, *C krusei*.[37] However, fluconazole obstruction in *C glabrata* is as often as possible an aftereffect of the outflow of multidrug efflux siphons; thus, cross-opposition might be seen with all azole antifungal agents.[38]

Pharmacokinetics

Antifungal Pharmacokinetic properties are regularly the most significant thought in medicate determination on the grounds that disabled GI tract work or decreased renal/hepatic medication freedom can significantly impact the wellbeing and viability of antifungal treatment.

A few classes of antifungal specialists must be regulated intravenously, including amphotericin B and the echinocandins, on the grounds that these operators are not adequately

consumed from the GI tract. This issue has been settled with the presentation of triazole antifungal specialists; be that as it may, the level of retention fluctuates significantly starting with one medication then onto the next. Fluconazole and Voriconazole both have oral bioavailability surpassing 90% and can be controlled regardless of food (Fluconazole) or ideally on a vacant stomach (Voriconazole).[39] Itraconazole cases and Posaconazole suspension expect food to draw out gastric habitation time to improve medicate disintegration, which isn't an issue with the oral Cyclodextrin plan of itraconazole that is managed on an unfilled stomach. Be that as it may, patients may like to take itraconazole arrangement with food given GI prejudice and the unpalatable lingering flavor of the solution.[40] Medication cooperations are another significant reason for pharmacokinetic fluctuation since co-administration of any triazole or Caspofungin with intense inducers of stage 1 (CYP) and stage 2 digestion (i. e, rifampin, phenytoin) can bring about low (fluconazole, caspofungin, Posaconazole) or imperceptible (itraconazole, voriconazole) circulatory system convergences of the antifungal operator and an expanded danger of treatment failure.[41] For the situation of itraconazole, voriconazole, and posaconazole, communications with powerful inducers of CYP3A4 can't generally be overwhelmed with higher antifungal medication doses.[42-45]

Pharmacokinetic sedate medication connections are additionally intensified by the way that some antifungal operators repress the freedom or digestion of different medications. Nephrotoxicity related to amphotericin B treatment (frequently quickened by calcineurin inhibitors, aminoglycosides, intravenous radiocontrast specialists, foscarnet, or forceful diuresis) will decrease the leeway of other really wiped out drugs.[46] Pharmacokinetic tranquilize sedate collaborations are generally hazardous, notwithstanding, with triazole antifungal operators since these operators restrain human CYP chemicals to differing degrees.[47,48] These communications can be perilous if not foreseen in patients accepting medications with a tight remedial list, for example, chemotherapeutic specialists, immunosuppressants, and some cardiovascular prescriptions.[49,50]

Pharmacodynamics

Antifungal specialists show various examples of movement in vivo (i.e., focus autonomous or fixation needy as dictated by the state of the portion reaction bend at clinically accomplished concentrations).[51] These examples of action in vivo can regularly be connected with the medication portion and the pathogen MIC to recognize dosing methodologies that expand

antifungal viability while decreasing the danger of harmfulness. Pharmacodynamic information may likewise be helpful for anticipating destinations of contamination where antifungal medications have a higher danger of treatment disappointment (i. e, cerebrospinal liquid, and vitreous liquid, pee) on the grounds that insufficient conveyance prompts incapable medication fixations.

Flucytosine shows focus autonomous Pharmacodynamic qualities in vitro and in vivo against Candida and Cryptococcus species; i. e, increments in serum sedate fixations over the pathogen MIC don't considerably expand the rate or degree of parasitic killing. In portion fractionation concentrates in creatures, the capacities of a dose routine to keep up serum tranquilize fixations over the MIC (percent of time more noteworthy than MIC of 20%-40%) was the best indicator of 5-FC movement against *Candida albicans*.[52] This acknowledgment drove to a limited extent to contemplates that pre-owned lower dosages of 5-FC (100 mg/kg day by day) in mix with higher amphotericin B treatment portions for *cryptococal meningitis*, despite the fact that Pharmacodynamic information for 5-FC in the treatment of *Cryptococcus neoformans* are limited.[53]

Triazole antifungal specialists have maybe the biggest collection of trial and clinical writing setting up a connection between's medication portion, creature MIC, and outcome. Experimental examinations in creatures and clinical investigations with fluconazole in the treatment of mucosal and intrusive candidiasis recommend that accomplishing a serum free-sedate AUC: MIC proportion of more noteworthy than 25 is the parameter most firmly connected to fruitful treatment.[54-56] Although less information is accessible for different triazoles and shape diseases, concentrates in creature models of aspergillosis likewise propose that the AUC: MIC proportion is the best indicator of treatment reaction to Posaconazole, with half endurance at absolute medication AUC: MIC proportions of 100 to 150 and maximal reactions at a proportion more prominent than 440 (free-tranquilize AUC: MIC proportion of roughly 8-25).[57,58]

Clinical preliminary information for candidal diseases is recommended that this Pharmacokinetic-Pharmacodynamic relationship might be useful for foreseeing treatment viability in humans,[59-61] and have shaped the reason for weakness testing breakpoints in Candida species. For instance, confines with fluconazole MICs of 16 or more prominent would be hard to treat with standard measurements of 6 mg/kg day by day. Consequently, separates with fluconazole MICs of 16 to 32 μg/ml are classified as "defenseless portion

subordinate" rather than "middle of the road" since they may, in any case, be treatable given higher day by day measurements of fluconazole are utilized (i.e. 12 mg/kg day by day or roughly 800 mg/d). Candida disengages with MICs more noteworthy than 64 μg/mL would require fluconazole measurements of 1600 mg/d or more prominent and consequently are named "resistant." Recent examinations utilizing epidemiological cut-off investigation of wild-type powerless and fluconazole-safe Candida species, be that as it may, have incited reevaluation of these pharmacodynamics-driven breakpoints because they may not be adequately delicate to identify rising obstruction, particularly among non–C glabrata isolates.[62] Therefore, new species-explicit MIC breakpoints for fluconazole have been proposed for *C albicans*, *C parapsilosis*, and *Candida tropicalis* (helpless, ≤2 μg/mL; vulnerable portion needy, 4 μg/mL; safe, ≥8 μg/mL) while keeping up current breakpoints for *C glabrata* (defenseless portion subordinate, ≤32 μg/mL; safe ≤64 μg/mL).

Chemistry of azoles

Azoles are a class of Five-membered Heterocyclic mixes containing a nitrogen molecule and in any event one other non-carbon iota (for example nitrogen, sulfur, or oxygen) as a major aspect of the ring.[63] their names start from the Hantzsch–Widman classification. The parent mixes are fragrant and have two twofold bonds; there are progressively decreased analogs (Azolines and Azolidines) with less. One, and just one, solitary pair of electrons from each heteroatom in the ring is a piece of the sweet-smelling holding in an azole. Names of azoles keep up the prefix upon decrease (e.g., Pyrazoline, Pyrazolidine). The numbering of ring particles in azoles begins with the heteroatom that isn't a piece of a twofold bond, and afterward continues towards the other heteroatom. Imidazole and other five-membered fragrant heterocyclic frameworks with two nitrogens are very regular in nature and structure the center of numerous biomolecules, for example, histidine

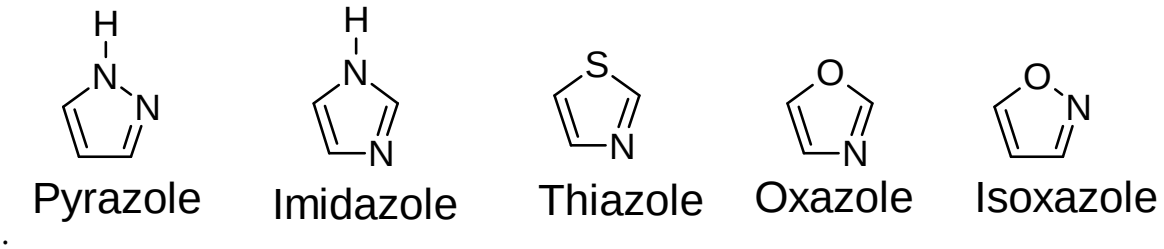
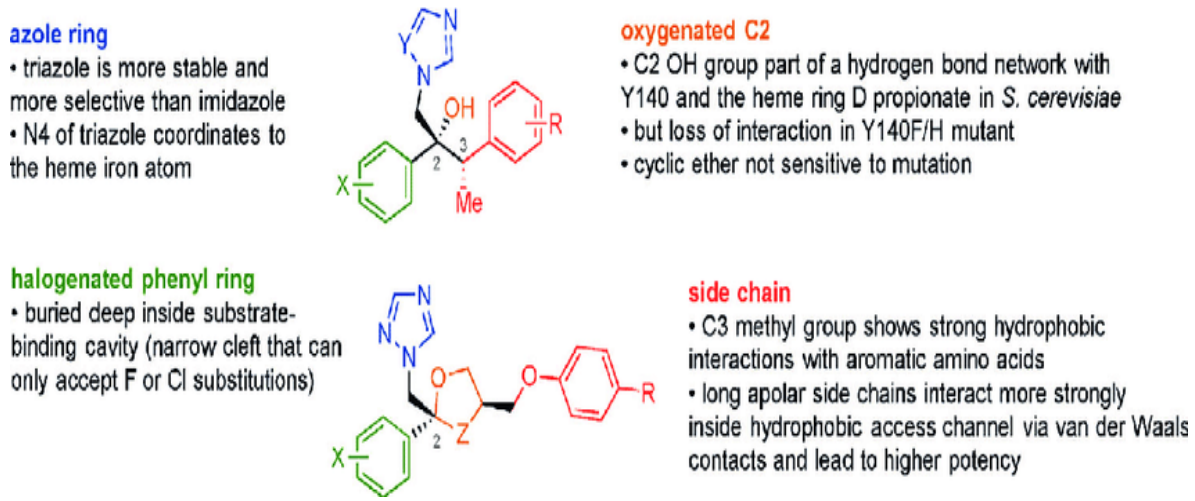


Figure 7: Five membered heterocyclic rings of azoles.

Sar of azoles



- The essential basic necessity for individuals from the azole class is a pitifully fundamental imidazole or 1, 2, 4-triazole ring fortified by a nitrogen-carbon linkage to the remainder of the structure.
- At the sub-atomic level, the amidine nitrogen atom (N-3 in the imidazol, N-4 in the triazoles) is accepted to spot to the heme iron of protein security cytochrome P450 to inhibit enactment of sub-atomic oxygen and forestall oxidation of steroidal substrates by the compound.
- The most powerful antifungal azoles have a few sweet-smelling rings, in any event one of which is halogen subbed (e.g., 2, 4-dichlorophenyl, 4-chlorophenyl, 2, 4-diflurophenyl), and other nonpolar practical gatherings.
- Just 2, &/or 2, 4 replacement yields successful azole mixes.
- The halogen particle that yields the most intense mixes are fluorine, albeit useful gathering, for example, sulfonic acids have been appeared to do likewise.
- Replacement at different places of the ring yields latent mixes.
- Presumably, the enormous nonpolar segment of these atoms impersonates the nonpolar steroidal piece of the substrate for lanosterol 14-demethylase, lanosterol, in shape and size.
- The nonpolar usefulness presents high lipophilicity to the antifungal azoles.
- The free bases are ordinarily insoluble in water yet are dissolvable in most natural solvents, such as ethanol.
- Fluconazole, which has two polar triazole moieties, is a special case, in that it is adequately water dissolvable to be infused intravenously as an answer of the free base.[64]

Future scope

Antifungal therapy widely used azole derivatives of heterocyclic five-membered contain nitrogen usually obtain by naturally and develop by a synthetic system they are used in the different-different field of science and the large number of another types azoles derivative are obtained by biomimetic or research different azole derivatives as like Pyrazole (I), Imidazole (II), Triazole (III), Isoxazole (IV), Oxadiazole (V), Thiazole (VI).[65-70]

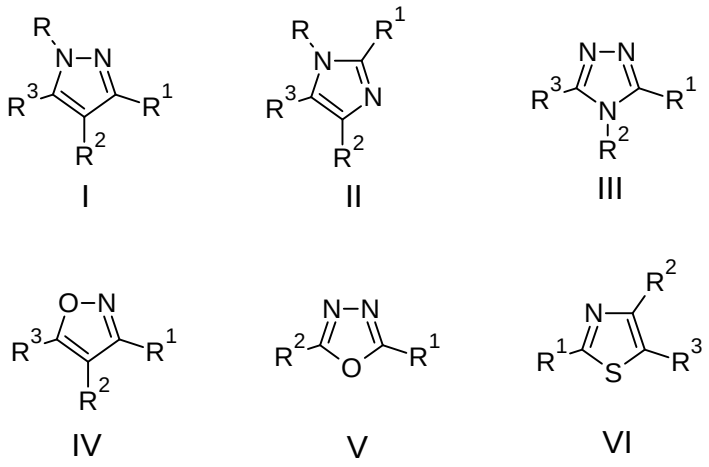
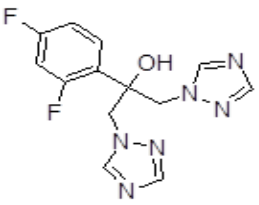


Figure 7: Azole derivatives.

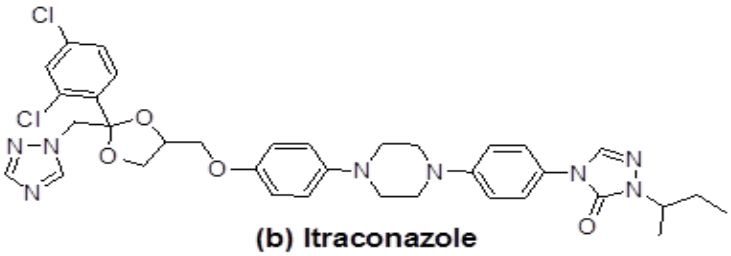
In which microbiology have seen about National Committee for Clinical Laboratory Standards NCCLS (NCCLS) are deal about the measurement of in vitro antifungal therapeutic effects. In their minimum inhibitory concentration is measured by Serial dilution on 96 -well micro test plate and the effects of the drug on microbes.[71]

Currently used azoles

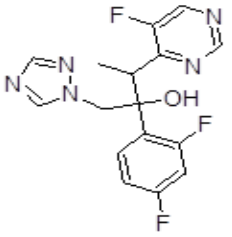
Azoles are mostly used in antifungal therapy they inhibit the growth of fungus and work by inhibiting dependent enzyme *lanosterol 14-alpha demthylase* they turn lanosterol to ergosterol, the main sterol of cell body decrease of ergosterol this is harmful to cell and created cell death. before one of the oldest classes of antifungal drugs used polyene category drug in which included Amphotericin B is used in antifungal they act as a bind to the ergosterol, and fungi cell membrane sterol are unique this is the mode of action.[72] However, its drawback is produced toxicity they are developed lipid mutation and reduces this problem.[73] at presently many drugs of azole (a) Fluconazole, (b) Itraconazole, (c) Voriconazole, (d) Posaconazole, and (e) Ravuconazole that are used for the antifungal and mostly azole have inhibited the growth of fungus (Fungistatic), but Voriconazole is destroying fungi broadly (fungicidal).[74]



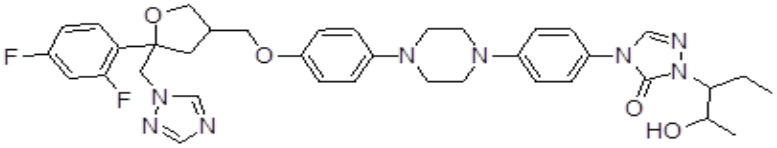
(a) Fluconazole



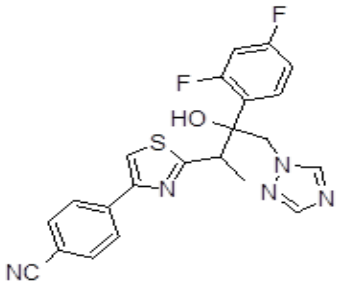
(b) Itraconazole



(c) Voriconazole



(d) Posaconazole



(e) Ravuconazole

Latest approaches for superficial fungal contamination: In which, some newer patented dosage forms like cream, methodical use (triazole, imidazole, allylamines, morpholine) are used to treat fungal infection and other skin inflammation and treatment based on their which type of infection, site of infection after applying medication gives a better effect on the disease they are best used in the treatment of superficial fungal infection and they are the time to change and improve. They are best for use on skin disorders like *Malassezia spp*, in atopic dermatitis, SD and change on the route of administration, delivery system and using a combination of a drug that increase the therapeutic effect.

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