

## ANTIFUNGAL DRUGS USED IN DENTISTRY

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### ABSTRACT:

Fungal infections are usually more difficult to treat than bacterial infections because fungal organisms grow slowly. Oral candidiasis, a frequent and important fungal condition of the oral cavity is caused by *Candida* species. There are few local factors that make the oral tissues susceptible to *Candida* infection. These factors include acid saliva, xerostomia, night use of prosthetic dentures, tobacco, carbohydrate rich diets and patients that receive radiotherapy and chemotherapy in maxillofacial structures and also associated with the use of broad spectrum antibiotics, corticosteroids, anticancer/immunosuppressant drugs, emergence of AIDS. Antifungal drugs are used in dentistry in the management of oral candidal infections. They are available as lozenges, gels, ointments and oral suspension for topical use. Systemic dosing may also be used when the infection is severe. Three groups of compounds are used. These are polyenes, imidazoles and triazoles. Amphotericin and Nystatin are polyenes that are not absorbed after oral administration. The imidazoles and triazoles achieve their antifungal action by inhibiting the synthesis of ergosterol and it results in decreased fungal replication. Maintenance of oral hygiene and early diagnosis of this condition is very important. This article reflects on clinical application of antifungal drugs in dentistry.

**Key words:** Antifungal drugs, Oral Candidiasis, Denture stomatitis, Clotrimazole, Nystatin.

### INTRODUCTION:

Fungi generally constitute a relatively small, proportion of oral microflora. The perfect fungi that divide by sexual reproduction are rarely isolated from oral cavity but occasionally found in infecting patients with advanced acquired

immunodeficiency syndrome. The perfect fungi causing oral infections are *Aspergillus*, *Geotrichium* and *Mucor* species. The imperfect yeasts such as *Candida* species which divide by asexual reproduction are found in the mouth. [1] The largest proportion of the fungal microflora in the human mouth is made

up of Candida species. Candida albicans are one of the components of normal oral microflora and around 30% to 50% people carry this organism. Rate of carriage increases with age of the patient. Candida albicans are recovered from 60% of dentate patient's mouth over the age of 60 years. There are nearly five types of candida species which are seen in the oral cavity. *Candida albicans*, *Candida tropicalis*, *Candida krusei* *Candida parapsilosis*, *Candida guilliermondii*. Among these five types, Candida albicans are commonly seen in the oral cavity. Candida albicans is a dimorphic fungus that causes severe opportunistic infections in humans.<sup>[2]</sup> There are three general factors which helps the Candida albicans infection to develop in the patient's body. They are: Immune status of the patient, Oral mucosal environment, Strain of Candida albicans. The main factors which increase susceptibility of oral candidiasis are: Immunosuppression, Endocrinopathies, Nutritional deficiencies, Malignancies, Dental prosthesis, Epithelial alteration, high carbohydrate diet, Infancy and old age, Poor oral hygiene, heavy smoking.<sup>[3,4]</sup>

### Classification of Antifungal drugs:

Antifungal drugs are used in both superficial and deep fungal infections classified as in different groups shown in Table: 1<sup>[5]</sup>

### Clinical application in dentistry:

Lehner has classified oral candidiasis as follows shown in Table: 2<sup>[6]</sup>

Newton has classified Denture- sore mouth as shown in Table: 3<sup>[7]</sup>

These conditions are treated by antifungal drugs (Nystatin, Amphotericin-B, Miconazole and Fluconazole) and disinfectants (0.2% Chlorhexidine gluconate mouth washes 3 or 4 times a day). Even though denture stomatitis is asymptomatic, it should be treated as it may act as reservoir for infections which can become extensive and lead to the resorption of the alveolar bone. The most effective treatment is the eradication and control of the microbial plaque.

### 1. Nystatin:

It is polyene antibiotic obtained from *Streptomyces noursei*.

Trade name: MYCOSTATIN

Preparation available:

Oral - 5, 00,000 unit tablets

Topical - 100,000 unit/gm cream and ointments, 100,000 units vaginal tablets. It is available currently for topical use in creams, ointment, suppositories, lotion, suspension, vaginal tablets, and oral pastille.

**Mechanism of action:** Depending upon concentration used, it can be either fungistatic or fungicidal agent. It binds to the ergosterol and increases the permeability of cell membrane facilitating pore formation. These microspore formation allow leakage of intracellular ions and macromolecule leading to cell death.

**Indication:**

**Oral candidiasis (Oral thrush):**

Nystatin is drug of choice. It is commonly used as topical agent to suppress Candida infection. It is not administered parentally as it is toxic for systemic use. Thrush is treated by holding 5 ml of nystatin suspension (for infants- 2 ml) in oral cavity for several minutes 4 times daily before swallowing. Alternative treatment is to retain vaginal tablet in the mouth until it dissolves, at least 4 times a day. Nystatin oral pastille (200,000 units) dissolved slowly in the mouth 5 times a day—can be mixed with glycerin. Mycostatin creams and ointments (1 lack units) may be used in candidiasis with angular cheilitis, stomatitis. Mycostatin oral rinse - 1 teaspoon of nystatin oral suspension (100,000unit/cc) mixed with ¼ cup of water is used as oral rinse for 3-4 times a day for 7-10 day

**Denture stomatitis (chronic atrophic candidiasis):**

0.2% chlorhexidine solution with Mycostatin tablet dissolves in it forming gel used mainly in such patients. In denture wearing patients, nystatin ointments are to be applied to the fitting surface of clean denture thoroughly and regularly and should be left out of mouth at night keeping it in 0.02% of sodium hypochlorite solution.

Nystatin tablets 500,000 units were allowed to dissolve in the mouth three times a day for 14 days. Bergendal and Isacson reported similar results by

treating denture stomatitis with nystatin powder, placed on the fitting surface of the denture; three times a day for 14 days. Nystatin is formulated for oral use as suspension or pastille. [8]

Lucio Milillo, Lorengo et al in 2005 had conducted a study of the efficacy of amorolfine anti-fungal varnish in Candida related denture stomatitis. They had done this to avoid the use of systemic antifungal agents in nystatin resistant cases. [12]

**Candidial Angular cheilitis:**

Treatment with Nystatin or Mycostatin yield good result.

**Adverse effect:** fever, chills, headache, hypotension, rashes, nausea, and vomiting.

**Contraindication:** Hypersensitivity reaction.

**2. Amphotericin-B:**

Amphotericin B is an antifungal antibiotic produced by *Streptomyces nodosus*.

Trade name:

Fungizone, Abelcet, Ambisome, Amphotec.

Preparation available:

Parenteral: conventional formulation: Fungizone 50 mg power for injection.

Lipid formulation: Abelcet -100 mg/20 ml suspension for injection. Ambisome-50 mg powder for inj. Amphotec-50,100 mg powder for inj.

Topical: 3% cream, lotion, ointment.

**Mechanism of action:**

It binds to the ergosterol. The sterol of cell membrane of fungi increases the permeability of cell membrane facilitating pore formation. These pore formation allow loss of cation, intracellular ions and loss of calcium leading to cell death. It acts as fungicidal at high concentration and fungistatic at low concentration. It is effective against numerous fungi and yeast like *Candida albicans*.

**Indication:**

**Oral candidiasis:** Used in Oral candidiasis (Oral thrush), acute atrophic candidiasis (antibiotic stomatitis), denture sour mouth (chronic atrophic candidiasis), chronic hyperplastic candidiasis (candidial leukoplakia).

- Amphotericin B is mostly applied topically in the form of ointment, suspension, drops, cream, and lotion. It is applied 2-3 times a day. Mystelicin elixir containing both tetracyclines vigorously swished in the mouth and then swallowed, 4-5 times for 2-1 weeks.
- In denture wearing patient, amphotericin B ointment applied to fitting surface of denture before it use.

**Adverse effect:** It is toxic drug causes impairment of renal and hepatocellular function, anemia, mental and neurological changes, renal toxicity. Chills, fever,

vomiting, headache, thrombophlebitis may occur if injected IV.

**3. Hamycin:**

It is polyene antibiotics obtained from *Streptomyces pimprina*.

Trade name: HAMYCIN, IMPRIMA

Preparation available: Topical- 4 lac unit/gm ointment, 5 lac unit vaginal ovules, 2 lac/ml suspension.

**Indication:**

Oral thrush (due to *Candida albicans*): Ointment or suspension is applied to the affected area of oral mucosa with sterile cotton 2-3 times a day for 7-10 days. It can also be given in cutaneous candidiasis, moniliasis and otomycosis caused by *Aspergillus*. Dose recommended is 10-20 mg/kg daily.

**Adverse effect:** Mild rashes, irritation.

**Contraindication:** Hypersensitivity.

**4. Natamycin:**

Trade name: NATAMYCIN, PIMAFUCIN

Preparation available: Topical - 5% suspension, 2% cream, 1% ointment and 25 mg vaginal tabs.

**Indication:**

- Oral thrush/ Oral candidiasis: Natamycin vaginal tab or ointment is applied on affected area of oral mucosa for several minutes 3-4 times daily

**Adverse effect:** Nausea, mild rashes occasionally.

## 5. Flucytosine (5-FC):

It is oral antifungal agent effective against systemic infection due to yeast and fungi.

Trade name - ANCOBON

Preparation available - Oral: 250, 500 mg capsule, 100 - 150 mg/kg/day in patient with normal renal function.

### Mechanism of action:

It has antifungal action. Susceptible fungal cell take up flucytosine, convert it to fluorouracil, which is converted to 5-fluorodeoxyuridylic acid which inhibit DNA and RNA synthesis. But human cells are unable to convert parent drug to its active metabolites, so it is relatively non-toxic.

### Indication:

It is mainly used as an adjuvant drug. Flucytosine is used in combination with itraconazole.

**Adverse effect:** Prolonged use with high doses cause leukopenia, thrombocytopenia, and anemia due to bone marrow depression, nausea, vomiting, and skin rashes.

## 6. Clotrimazole:

It is used exclusively as topical agent. It is toxic on parental administration.

Trade name: MYCOBAN, LOTRIMIN, MYCELEX, SURFAZ, CLOTRIN, CLODERM, CANDID.

Preparation available:

Topical: Mycoban Gel 12% (30 gm), Gynostatum vaginal tab, 1% vaginal

cream, lotion, solution. Oral: 100 mg, 200 mg, 500 mg tab.

### Mechanism of action:

It inhibits the synthesis of ergosterol by binding to catalytic haem ion of fungal cytochrome resulting in damage to cell membrane of fungi.

### Indication:

Candidiasis caused by *Candida albicans*, oral candidiasis, cutaneous candidiasis.

For oropharyngeal candidiasis 10 mg troche of clotrimazole is allowed to dissolve in the mouth 3-4 times a day, or the lotion/ gel is applied/ swirled in the mouth for as long as possible.

It is also effective in skin infections caused by Corynebacteria.

**Adverse effect:** Local burning or stinging, skin irritation, rash, hypersensitivity.

**Contraindication:** 1st trimester of pregnancy.

## 7. Econazole:

It is antifungal agent mainly used topically.

Trade name: ECANOL, SPECTAZOLE, ECODERM, ECONAZOLE

Preparation available: Topical: 1% cream - 10 gm.

**Mechanism of action:** same as Clotrimazole.

**Indication:**

Treatment for trichomoniasis-1% ointment, 150 mg vaginal tablets is applied to affected area of skin or oral mucosa twice a day for 7-10 days.

Mucocutaneous candidiasis: It is used as an oral rinse, cream, ointment as well as suspension. Vaginal tab dissolved in ¼ cup of water and used as oral rinse for oral candidiasis.

**Adverse effect:** Local burning or stinging, skin irritation, rash.

**8. Miconazole:**

It is used as topical antifungal agent. It is more toxic than ketoconazole.

Trade name: MICOGEL, MONISTAT, MICATIN, ZOLE, DAKTARIN

Preparation available:

Topical: ointment 2%-15 gm, lotion 2%-15 ml, powder 2%-15 gm, cream 2%-15 gm, gel 2%-15 gm, vaginal suppositories- 100, 200 mg.

Mechanism of action: same as Clotrimazole.

**Indication:**

- Severe systemic fungal infection: In adult, 1200 to 2400 mg/day in divided doses.
- Cutaneous candidiasis: Applied cream, ointment to be affected area twice daily for 7days.

- Systemic mycosis: Miconazole is used by intravenous route (Monistat).
- Ocular infection: Topical (1%) for every hours and subconjunctival injection of 5 mg miconazole (1%) MICOPTIC OPICOPS once/twice a day.

**Adverse effects:** Chills, fever, itching, nausea, rashes, phlebitis, anemia, irritation to skin.

**9. Ketoconazole (KTZ):**

It was first orally effective azole antifungal agent used in the treatment of systemic fungal infection. It is less toxic than Amphotericin B. The oral absorption of KTZ is facilitated by gastric acidity because it is more soluble at lower pH.<sup>[9, 10]</sup>

Trade name: NIZRAL, TOCON, FUNGICIDE, FUNAZOLE, KETOVATE, HYPHORAL

Preparation available:

Oral- Tab 200 mg, Topical: 2% cream, and shampoo.

Mechanism of action: same as Cotrimazole.

**Indication:**

- Mucocutaneous candidiasis: Tab 200 mg once a day is very effective.
- Candidiasis, seborrheic dermatitis: Oral dose of 200 mg daily for 2-3 weeks can be given. Ketoconazole (Nizoral) available as a cream for topical treatment. 3) Shampoo 1%

is used for seborrheic dermatitis (Nizoral AD Shampoo).

**Adverse effect:**

Nausea, vomiting, loss of appetite, giddiness, headache, rashes, photophobia, and paresthesia. It interferes with biosynthesis of adrenal and gonadal steroid hormone producing gynaecomastia, infertility, menstrual irregularities and GIT upset.

**10. Fluconazole:**

It is new antifungal drug which is more water soluble and has good penetration into cerebrospinal fluid, ocular fluid, vaginal tissue and saliva. It can be administered intravenously or orally.

Trade name: SYSCAN, DIFLUCAN, ZOCON, FORCAN, FLUZON

Preparation available:

Oral 50, 100, 150, 200 mg tablets, Topical: powder for 10, 40 mg/ml suspension. Parenteral-2 mg/ml in 100 and 200 ml vial.

**Mechanism of action:**

It acts by inhibiting the enzyme demethylase resulting in the damage to fungus cell membrane. It has fungistatic action.

**Indication:**

Mucosal candidiasis/mucocutaneous candidiasis: Ketoconazole can be given orally in the dose of 50-100 mg daily for 14-30 days or intravenously. For mucosal infection, topical application may useful.

Systemic candidiasis: For systemic infection, 400 mg of ketoconazole either orally or intravenously on first day then 200-400 mg once a day for 15-30 days. For children: 3-6 mg/kg BW daily in severe life threatening infection in over 1year.

- Prophylactic agent for bone marrow transplantation recipients and AIDS patient. Prophylactic use of fluconazole to reduce fungal infection is used.
- Oral fluconazole (150 mg/ day for 2 weeks) is highly effective in oropharyngeal candidiasis, but is reserved for cases not responding to topical antifungals.

**Adverse effect:** Nausea, headache, abdominal pain.

**11. Itraconazole:**

It is newer antifungal drug which is administered orally. Its efficiency is enhanced in combination with flucytosine. [9,10]

Trade name: ITROLE, CANDITRAL, SPORANOX, CANDISTAT, ITASPOR, FLUCOVER

Preparation available:

Oral- 100 mg, 200 mg Capsule.

Topical: 10 mg/ml solution, Parenteral: 10 mg/ml for IV infusion.

**Mechanism of action:** same as Fluconazole.

**Indication:**



Oropharyngeal candidiasis: Oral liquids and intravenous preparation are quite effective in the dose of 200 mg capsule/tablets twice daily for at least 6 month, yields good results.

**Adverse effect:**

Peripheral neuropathy, headache, dizziness, allergic reaction, jaundice, hepatotoxicity.

**12. Newer Antifungal drugs:** <sup>[11]</sup>

**Silver sulfadiazine (SSZ):** SSZ has broad spectrum of antifungal activity against *Candida*, *Aspergillus*, *Fusarium*, and other fungal infections of the eye.

Trade name: APLICAPS.

Preparation: Topical: 1% suspension, Oral: 250 mg tablets.

**Indication:**

It is used in fungal infection of the eye caused by *Candida*, *Aspergillus*, and *Fusarium*. 1% suspension is used, 5 times a day. SSZ is also available in 1% eye drops and ointment 1% - applied topically 4-5 times daily.

**13. Ciclopirox olamine:**

It is newer antifungal agent with high cure rates. It has good penetration power.

Trade name: LAPROX, BATRAFEN, OLAMIN

Preparation: 1% cream, lotion.

**Indication:**

- It is used in Tinea infections,

- Dermatophytosis, Candidiasis: Topical application of cream or lotion over skin and oral mucosa, 4-5 times/ day yield good results due to good penetration power.

**14. Voriconazole:**

It is newest triazole to enter clinical trials. It is available in an intravenous and oral formulation. Recommended dosage is 400 mg/day. It has broad spectrum of action mainly against *Candida* species. Voriconazole is most effective than itraconazole in candidial infection. <sup>[11]</sup>

**Indication:**

Oral thrush: Orally or intravenously administered in the dose of 400 mg/day. Mucocutaneous preparation: Topical 10% ointment, cream.

**15. Brazilian Green Propolis:**

Propolis is a resinous material collect by bees from various plants, and this chemical composition depends on its origin area. Extract of Propolis contains a wide variety of components like flavonoids and phenolic acids. The flavonoids in Propolis, mainly pinocembrin, have been considered to be responsible for its inhibitory effect on *Candida*. Antifungal activity is one of the most extensively investigated biological actions of Propolis. Recently a study was done to comparison of the efficacy of a new form of Brazilian green propolis, using a formula propylene glycol contrasting it with miconazole gel in the topical treatment of *Candida*-associated denture stomatitis. The overall results



showed that propylene glycol Brazilian green propolis has an antifungal activity similar to miconazole, in the *C. albicans* colonies decrease and in the erythema reduction of patients with Candida-associated denture stomatitis. Brazilian green propolis that has antifungal properties is a safe, affordable, and natural product without well-known side effects up to now.<sup>[12]</sup>

#### 16. Amorolfine:

Amorolfine varnish is a medicine used in the topical treatment of onychomycosis caused by dermatophytes, yeasts and moulds. The varnish contains 5% w/v amorolfine (as hydrochloride) as active ingredient in an ethanol base. The active substance Amorolfine belongs to the morpholines derivatives class of antifungal substances. It has got antifungal and fungistatic effect. The ingredients of Locetar 5% varnish are amorolfine chloride, copolymer of methacrylic acid, triacetin, butyl acetate, ethyl acetate and ethyl alcohol.<sup>[13]</sup>

Lucio Milillo, Lorengo et al had conducted a study of the efficacy of amorolfine antifungal varnish in Candida related denture stomatitis. They had done this to avoid the use of systemic antifungal agents in nystatin resistant cases.<sup>[13]</sup>

#### Antifungal action of antiseptic and disinfecting agent:

**Listerine** : An in vivo programme involving the use of Listerine\*\*\* antiseptic (ethanol 0.26 mL, benzoic acid 1.5 mg, thymol 0.63 mg, eucalytol 0.9 mg per mL) and

Mycostatin as mouth rinses and denture soaks over a period of 28 days resulted in a significant reduction in palatal inflammation and candidal colonization of dentures and palatal mucosa, although denture plaque scores did not differ significantly. In another study a 0.2% chlorhexidine gluconate mouth rinse used three times daily significantly reduced plaque, but there was no significant effect on the number of Candida organisms.<sup>[14,15]</sup>

**Peridex**: Epstein has described the use of Peridex containing chlorhexidine gluconate, in the treatment of oral candidosis. The drug is a broad spectrum mouthrinse which is adsorbed on the surfaces of microorganisms, increasing permeability of cell membranes and causing precipitation of cytoplasmic contents. It was found that chlorhexidine bound to salivary pellicles as well as hard tissues in the oral cavity, resulting in chlorhexidine titres in saliva for 12 hours or more after rinsing. Although effective in the treatment of oral candidosis, unpleasant side effects included staining of the tooth surfaces and a bitter taste.<sup>[16]</sup>

Lal et al. investigated the use of chlorhexidine gluconate in the form of Peridex both as a mouth rinse and a denture soak in the treatment of denture stomatitis. The study was for a period of 24 days and Peridex oral rinse containing 0.12% chlorhexidine gluconate was used twice daily and dentures soaked overnight in Peridex solution. It was found that chlorhexidine completely eliminated *C. albicans* on the acrylic resin denture

surface and significantly reduced palatal inflammation.<sup>[17]</sup>

### Guidelines for treatment and prophylaxis of invasive fungal diseases:<sup>[18, 19]</sup>

Patient selection criteria may include:

- Clinical history, signs and symptoms.
- Imaging studies
- Microscopic findings in suitable specimens.
- Rapid diagnostic tests (e.g. exfoliative cytology, tissue biopsy, antigen or nucleic acid detection tests, liver function test, and renal function test)
- Culture results from suitable specimens.
- Histological findings.
- Always continue the treatment for 2 weeks after resolution of the lesions. When the topical therapy fails then one has to start systemic therapy because failure of drug response is the initial sign of underlying systemic disease. Follow-up appointment after 3 to 7 days is important to check the effect of drugs. Main Goals of treatment are :
  - To identify & eliminate possible contributory factors
  - To prevent systemic dissemination

- To eliminate any associated discomfort
- To reduce load of candida
- Treatment options are mainly categorized in to two lines, primary & secondary line of treatment

#### Primary line of treatment:

Nystatin is the drug of choice as a primary line of treatment. Usually for the mild and localized candidiasis this primary line of treatment is used other drugs includes Clotrimazole which can be taken as is Lozenges and Amphotercin B as oral suspension.<sup>[4, 5]</sup>

#### Second line of treatment:

- The second lines of treatment are used for severe, localized, immunosuppressed patients and patients who respond poorly to primary line of treatment. Drugs mainly used in second line of treatment are:

1. Ketoconazole
2. Fluconazole
3. Itraconazole

- Drug Interactions and Adverse Effect :<sup>[20]</sup>
  - Warfarin
  - Interaction with fluconazole, ketoconazole, itraconazole
  - Increase blood levels and risk of bleeding

- Monitor INR in patients (3.5 INR safe) effects
- Drug-disease interactions :
  - Prolonged use of systemic fungals may result in renal or hepatic dysfunction
  - Administer fluconazole, ketoconazole, or itraconazole with caution in patients with hepatic disease or when taking other hepatotoxic medications (APAP).
- Review

**Summary of Antifungal drugs:** Shown in Table: 6<sup>[10]</sup>

### CONCLUSION:

Candida species, although constituting only a minor proportion of the oral

microbiota, possess certain characteristics that are associated with their pathogenicity in medically and immunocompromised hosts of the oral candidal infections. Denture, oral hygiene and management of adverse medical conditions should be the primary goal of treatment. This should go hand in hand with the application of topical antifungal agents particularly those in the cream or gel form for better patient's compliance. Candida associated denture stomatitis is the commonest and because of the multifactorial nature of the disease, management is complex. Recent research has investigated plaque control, removal of dentures at night, the use of antiseptic and antimicrobial agents, antifungals and microwave irradiation as factors to consider in the treatment of candida associated lesion as: denture stomatitis, candidal leukoplakia and angular cheilitis.

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**TABLES:**

**TABLE: 1** Classification of Antifungal drugs

ANTIBIOTICS : [POLYENE]	<ul style="list-style-type: none"> <li>▪ Amphotericin B</li> <li>▪ Nystatin</li> <li>▪ Hamycin</li> <li>▪ Natamycin</li> </ul>
HETEROCYCLIC BENZOFURAN	<ul style="list-style-type: none"> <li>▪ Griseofulvin</li> </ul>
ANTIMETABOLITES	<ul style="list-style-type: none"> <li>▪ Flucytosine</li> </ul>
AZOLES	<p>Topical:</p> <ul style="list-style-type: none"> <li>▪ Clotrimazole</li> <li>▪ Econazole</li> <li>▪ Miconazole</li> </ul> <p>Systemic:</p> <ul style="list-style-type: none"> <li>▪ Ketoconazole</li> </ul>
TRIAZOLES	<p>Systemic</p> <ul style="list-style-type: none"> <li>▪ Fluconazole</li> <li>▪ Itraconazole</li> </ul> <p>Allylamine</p> <ul style="list-style-type: none"> <li>▪ Terbinafine</li> </ul>
OTHER TOPICAL AGENTS	<ul style="list-style-type: none"> <li>▪ Tolnaftate</li> <li>▪ Undecylenic acid</li> <li>▪ Benzoic acid</li> <li>▪ Cyclopiroxolamine</li> <li>▪ Quiniodochlor</li> <li>▪ Sodium thiosulfate</li> </ul>

**TABLE: 2** Classification of oral candidiasis

Primary oral candidiasis Acute	<ul style="list-style-type: none"> <li>▪ Acute pseudomembraneous candidiasis (thrush).</li> <li>▪ Acute-atrophic Candidiasis-Antibiotic sore-mouth.</li> </ul>
Chronic	<p>a.Chronic-atrophic Candidiasis</p> <ul style="list-style-type: none"> <li>▪ Denture-Stomatitis (Denture-sore mouth)</li> <li>▪ Angular chelitis</li> <li>▪ Median rhomboid glossitis</li> </ul> <p>b.Chronic hyperplastic candidiasis</p>

Secondary oral candidosis <ul style="list-style-type: none"> <li>▪ Oral manifestation of systemic mucocutaneous candidosis</li> </ul>	<ul style="list-style-type: none"> <li>▪ Familial mucocutaneous candidiasis</li> <li>▪ Diffuse chronic mucocutaneous candidiasis</li> <li>▪ Familial mucocutaneous candidiasis</li> <li>▪ Chronic granulomatous disease</li> <li>▪ Candidosis endocrinopathy syndrome</li> <li>▪ Acquired immune deficiency syndrome (AIDS)</li> </ul>
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**TABLE -3** Types of denture sore mouth

<b>TYPE-1</b>	<b>A localized simple inflammation or pin point hyperemia</b>
<b>TYPE-2</b>	A more diffuse erythema involving a part or the entire denture covered mucosa and hard palate
<b>TYPE-3</b>	A granular type (papillary hyperplasia) commonly involving the central hard palate and alveolar ridges.

**TABLE - 4** Topical Antifungal drugs for the management of oral candidiasis

Drug	Brand name	Form	Dosage	Adverse effect	Monitoring
<b>Nystatin</b>	Nystat ,Mycostatin	Cream and ointment (100,000U/g)	Apply to the affected area 3-4 times/day	Negligible absorption from gastrointestinal tract  Nausea, vomiting, diarrhea, stomach pain, contact dermatitis.	Liver function test
		Pastille(100,000 U/ml	Dissolve 1 pastille slowly after meals 4times/day for 7 days		
		Oral suspension(100,000U)	Apply after meals for 4times/day for 7 days and continue use for several days after post clinical healing.		
		Powder(50milli on U)	Sprinkle on tissue contact area of denture.		

		Troche(200,000 U)	200,000-400,000 U 4-5 times/day		
<b>Clotriamzole</b>	Mycelex, Gyne- Lotrimin, Candid	Cream	Apply to the affected area for 2-3 times/day for 3-4 week.	Abnormal liver function test,nausea,vomiting,local mild burning,irritation,stinging	Liver function test
		Solution	5ml 3- 4times/day for 2week		
		Troche	minimum. 10 mg troche: dissolve slowly over 15-30 minutes		
<b>Ketoconazole</b>	Nizoral	Cream	2% of cream rub gently into the affected area 1-2 times daily.	Irritation, pruritus, stinging, Avoid contact with eyes.	Liver function test
		Tablet	200-400mg tablet taken once or twice daily with food for 2 weeks		

**TABLE -5** Systemic Antifungal drugs for the management of oral candidiasis

Drugs	Brand name	Form	Dosage	Adverse effect	Monitoring
Fluconazole	Diflucan	Capsules	50-100mg capsules once daily for 2-3 weeks	Headache,nausea,abdominal pain,vomiting,rash, taste perversion, dyspepsia, diarrhea,left ventricular dysfunction,congestive,anaphylactic reaction	Liver and renal function tests, potassium
		Tablet	200mg on day1 then 100mg daily for 7-14 day		
		Powder	Powder for oral suspension 10mg/mL		



Itraconazole	Sporanox	Capsules	100mg capsules taken daily immediately after meals for 2 weeks.	Nausea, edema, hypertension, headache, fever, dizziness, rash, pruritus, hyperkalemia, libido, hepatitis, liver dysfunction, adrenal suppression, steven-johnson syndrome	Liver function tests after 1 month of treatment
		Solutions	10mg/ml : 100-200mg/10ml once a day for 1-2 wk; if refractory to fluconazole		
Ketoconazole	Nizoral	Tablets	200-400 mg/d as single dose for 7-14 days	Hypersensitivity to azole drugs, Pruritus, nausea, vomiting, abdominal pain, gynecomastia, headaches, hemolytic anemia, hepatotoxicity, impotence, leukopenia, photophobia, somnolence, thrombocytopenia	Liver function test

**TABLE: 6** Summary of Antifungal drugs

Antifungal drugs	Dosage and duration (continue for at least 48 hours after lesions have cleared)	Possible drug interactions and contraindications
<b>Chlorhexidine</b>	0.12-0.2% mouth rinse twice daily	Tooth staining, especially if the patient drinks tea, coffee or red wine
<b>Amphotericin</b>	10mg lozenge, 100mg/ml suspension, 10-400 mg 6-hourly for at least 14-21 days	Topical use - no problems
<b>Amphotericin (i.v.)</b>	0.5mg/kg for at least 10-14 days	Expensive. Nephrotoxicity, arrhythmias, neuropathies, anaphylactoid reactions. Avoid in pregnancy. Liposomal amphotericin may be safer
<b>Nystatin (topical)</b>	500 000IU lozenge, 100 000IU pastille, 100 000IU per ml of suspension. 100 000IU 6 hourly for at least 14-21 days. suspension contains sucrose	Topical use often no problems but may be unpleasant taste, nausea or gastrointestinal disturbance.
<b>Clotrimazole (topical)</b>	10mg 6-hourly for at least 14 days. Contains sucrose. Available in INDIA	Difficult to dissolve if mouth dry
<b>Miconazole (topical)</b>	250mg tablet, 25mg/ml gel. 250mg 6-hourly for at least 14-21 days.  50mg/g denture lacquer; apply Weekly for at least 2 weeks.	May interact with many drugs, including antidiabetic drugs, anticoagulants, phenytoin, midazolam, cyclosporin, cisapride and terfenadine. Avoid in pregnancy, porphyria. May impair oral contraceptive. Even topical agent may be absorbed systemically.
<b>Fluconazole</b>	50-200 mg/day for at least 14 days	May interact with many drugs, including

<b>(oral)</b>		antidiabetic drugs, anticoagulants, phenytoin, midazolam, ciclosporin, zidovudine, terfenadine, cisapride. Avoid in pregnancy, porphyria. May sometimes be hepatotoxic and myelosuppressive. Expensive. Avoid in pregnancy, infants, renal disease. Less toxic than ketoconazole
<b>Itraconazole (oral)</b>	100–200mg/day for at least 14 days. 10mg/ml liquid 10ml twice daily for at least 14 days.	May interact with many drugs, including digoxin, sertindole, anticoagulants, phenytoin, midazolam, ciclosporin, simvastatin, terfenadine, cisapride. Avoid in cardiac disease, pregnancy, and porphyria. Expensive. May impair oral contraceptive
<b>Voriconazole (oral)</b>	200–400mg/day for at least 14 days.	For fluconazole-resistant <i>C. albicans</i> or <i>C. krusei</i> infections. Contraindicated in cardiac disease, liver disease, and pregnancy. May Prolong QT interval. May cause nausea, neuropathy, rash. Interacts with terfenadine, cisapride and astemizole
<b>Casposungin</b>	IV infusion 50mg daily.	For fluconazole-resistant <i>C. albicans</i> . Contraindicated in cardiac disease, liver disease, and pregnancy. Adverse effects including anaphylaxis. Interacts with ciclosporin and tacrolimus.