DRUG PROFILE

PVP IODINE

Introduction:

Povidone iodinated is a complex of iodine and povidone. It contains not less than 9% of available iodine. From this complex iodine is released for prolonged time. Concentration range of PVP-iodine between 3.75 -2500 ppm kill the Candida strain between 10 to 120 seconds.

PVP-iodine and their preparation are official in USP, European pharmacopoeia and are recognized as effective broad spectrum biocidal agent. The in vitro biocidal activity has been studied for years against bacteria, yeast, moulds, viruses, fungi, protozoa, actinomycetes and rickettsia.

Eleven product contain PVP-iodine were tested for their ability to inactivate HIV virus in cell culture system. All of the products completely inactivated the virus at PVP-iodine concentration greater than 0.5%. Usage of PVP-iodine has significantly reduced the irritancy and toxicity with iodine use and thus being used worldwide effectively.

Compared to other preparations, PVP-iodine exhibits markedly lower oral toxicity. Consequently, the accidental ingestion of PVP iodine solution is much less
hazardous that from equal amounts of available iodine solutions. For this reason, PVP-iodine solutions do not require the hazardous, poisonous warning labels on bottle that iodine products must have.

Moreover, animal and exposure tests have revealed virtually no skin reactions to PVP-iodine, and only very mild transitory effects on mucous membranes.

**General properties:**

Povidone iodine was introduced to the pharmaceutical market as an antiseptic agent in the fifties and is as effective as iodine itself against a broad spectrum of disease causing microorganisms. It differs from iodine in that it is less irritating to the skin and does not require iodides or alcohol to dissolve. Additionally povidone iodine stains are water washable. Early promotional materials refer to PVP iodine as “tamed iodine” because of its safety. Furthermore, the poison label required for iodine products are not necessary in commercial preparations contains PVP iodine.

♦ Broad spectrum biocidal activity  
♦ detoxified iodine  
♦ No detectable vapour pressure  
♦ Water soluble  
♦ Film forming capacity  
♦ Stable complex

At the same time, PVP iodine is safer and easier to use than classic iodine preparations and has low system toxicity. The prolonged non selective antimicrobial action of PVP iodine is unparalleled for surface microbiocidal activity and particularly effective in treating mixed infection. Its effectiveness has been clinically proven for all types of topical applications in both human and veterinary medicine.

**Action:**
PVP iodine is a loose complex of elemental iodine with a neutral, amphipathic organic compound, poly vinyl pyrrolidone, which serves as a sustained release reservoir of iodine. The carrier augments dispersibility and penetrate povidone iodine is a topical microbial antiseptic which essentially retains the broad spectrum activity of iodine, yet is virtually free from the undesirable feature associated with tincture of iodine and lugol’s solution. Iodine is bactericidal, sporicidal, fungicidal, protozoacidal, cysticidal and virucidal, gram-positive and gram-negative bacteria are about equally affected.

**Pharmacology:**

Elemental iodine has a very broad antimicrobial spectrum: bacteria, viruses, bacteria endosperm, fungi, and protozoa’s are destroyed through oxidative interaction and direct iodination of biological macromolecules. However, there have been reports of certain resistant germs. Povidone-iodine (synonym-PVP-iodine) is an iodophor, i.e. it is a labile complex of iodine with the polyvinylpyrrolidone, from which iodine is continuously delivered. Only this free iodine has antimicrobial activity. In iodophors there is a complex relationship between the concentration of the solution and the concentration of free iodine, so that e.g. through the dilution of a 10% solution with a rate of 1:10 more free iodine is released from the complex and the antimicrobial activity is increased.

**Indications:**

Povidone-Iodine solutions in water or alcohol are better tolerated than iodine solutions with comparable efficacy. Considering the necessary time of application and the correct dilution povidone-iodine is suitable for hand disinfection, surgical hand disinfection, as well as preoperative and pre-puncture skin disinfection. However, compared to chlorohexidine the latter is normally more effective. Povidone-iodine is
further more used for the treatment of burns and of different lesions decubitus and leg ulcers etc). Specialist’s opinions are divided on the indications. In any case, silver sulfadiazine is more effective for burns. In special preparations it is available for the therapy of inflammations in the mouth and pharynx and for vaginitis. For these indications there have only been limited comparisons with alternatives. Candidal or trichomonal infections of the vagina undoubtedly better treated specifically. The use of povidone iodine is particularly disputed for the irrigation of cavities.

Contraindications:

Hypersensitivity to iodine, thyroid diseases, renal failure, burns covering large surfaces (more than 20% of the body surface) pregnancy, nursing, and neonates than 6 months.

Cautions:

All povidone iodine preparations also contain a detergent in addition to the agent little is known about the tolerance of the detergents.

Adverse Reaction

Severe complications are rare and only infrequently occur following application on intact skin. Extended long term treatment and repeated irrigation of wounds and cavities can provoke abnormal thyroid gland function, hepatic or renal insufficiencies, metabolic acidosis, chemical peritonitis, convulsions, Neutrogena, etc. The plasma concentration of thyroid gland hormones can rise. In infants one must expect considerable iodine desorption and the respective consequences following application on the skin local irritation with a burning sensation and pruitus occasionally occur, contact eczemas are rare.

Interaction: Concomitant administration of silver sulfadiazine or chlorhexidine partial inactivation possible.
Stability: PVP-iodine can be stored in powdered form without significant iodine loss. Samples kept for three years at 65°C in glass stoppered bottle without tape or seal showed only 0.5% maximum loss of available iodine. The product should however be protected from moisture.

Compatibility:

PVP-iodine dosage forms have been compounded successfully as powders, tablets, liquid lotions, ointments, gels and sprays. If the vehicle or base reacts with iodine then the available iodine in the final preparation must be determined, since the germicidal activity of the finished product is dependent on the iodine, not the iodide content. PVP-iodine systems should be mildly acidic since alkaline solutions, including ammonia, and reducing agents lower the available iodine which in turn, results in lower antiseptic activity. PVP iodine is compatible with steel, wool and plastic but reacts with silver.

Health Hazards:

Acute: It is safe if used as a topical antimicrobial agent. Over exposure may cause local irritation to the skin can be absorbed through broken skin or lungs.

High concentration in blood may cause thyroid disorder, renal disturbances, and Acidosis and electrolyte disturbances.

Precautions:

Spills should be cleaned as soon as possible and washed with dilute ammonia (or) dilute sodium thiosulfate solution and large amount of water.
Avoid breaking vapours (or) mists. Do not get in eyes, on skin (or) on clothing. Wash thoroughly after handling and before eating (or) drinking. Removing contaminated clothing promptly.

Keep out of reach of children.

Emergency First Aid:

Eye – immediately wash with running water for 5 minutes. Get medical attention if irritation persists. Skin – avoid prolonged contact with excess wet solution. If irritation develops, get medical attention, ingestion – if swallowed, do not induce vomiting. Drink several glasses of water or milk. Obtain immediate medical attention. In half – if fumes cause respiratory discomfort, move to fresh air.

CICLOPRIOX OLAMINE

Definition: 6-cyclohexyl-1-hydroxy-4-methylpyridin-29(1H)-one and amino ethanol.

- Ciclopriox 76.0% to 78.5%
- 2-aminoethanol 23.3%

Molecular Formula: C_{14}H_{24}N_{2}O_{3}

Characters: A White or Pale Yellow, Crystalline Powder

Solubility: Sparingly soluble in water, very soluble in alcohol and in methylene chloride, slightly soluble in ethyl acetate, practically insoluble in cyclohexane.

pH: 8 to 9

Storage: Protected From Light

Drug Category: Antifungal Agents

Dosage Forms: Topical solution (8%)

Indications
Used as a topical treatment in immuno competent patients with mild to moderate onychomycosis of fingernails and toenails without lunula involvement, due to *Trichophyton rubrum*.

**Fig 12:** Structure of Cicloprior Olamine

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**Pharmacology**

Ciclopirox is a broad-spectrum antifungal medication that also has antibacterial and anti-inflammatory properties. Its main mode of action is thought to be its high affinity for trivalent cations, which inhibit essential co-factors in enzymes. Ciclopirox exhibits either fungistatic or fungicidal activity in vitro against a broad spectrum of fungal organisms, such as dermatophytes, yeasts, dimorphic fungi, eumycetes, and actinomycetes. In addition to its broad spectrum of action, ciclopirox also exerts antibacterial activity against many Gram-positive and Gram-negative bacteria. Furthermore, the anti-inflammatory effects of ciclopirox have been demonstrated in human polymorphonuclear cells, where ciclopirox has inhibited the synthesis of prostaglandin and leukotriene. Ciclopirox can also exhibit its anti-inflammatory effects by inhibiting the formation of 5-lipoxygenase and cyclooxygenase.

**Mechanism of Action**
Unlike antifungal such as itraconazole and terbinafine, which affect sterol synthesis, ciclopirox is thought to act through the chelation of polyvalent metal cations, such as Fe$^{3+}$ and Al$^{3+}$. These cations inhibit many enzymes, including cytochromes, thus disrupting cellular activities such as mitochondrial electron transport processes and energy production. Ciclopirox also appears to modify the plasma membrane of fungi, resulting in the disorganization of internal structures. The anti-inflammatory action of ciclopirox is most likely due to inhibition of 5-lipoxygenase and cyclooxygenase.

**Absorption**

Rapidly absorbed after oral administration. Mean absorption of ciclopirox after application to nails of all twenty digits and adjacent 5 millimeters of skin once daily for 6 months in patients with dermatophytic onychomycoses was less than 5% of the applied dose. Ciclopirox olamine also penetrates into hair and through the epidermis and hair follicles into sebaceous glands and dermis.

**Toxicity**

Oral LD$_{50}$ in rat is $>10$ ml/kg. Symptoms of overexposure include drowsiness and headache.

**Biotransformation / Drug Metabolism**

Glucuronidation is the main metabolic pathway of ciclopirox.

**Contraindications**

Penlac® nail lacquer Topical Solution, 8%, is contraindicated in individuals who have shown hypersensitivity to any of its components.

**Drug Interactions:** No information provided.
**ITRACONAZOLE**

**Definition:** Itraconazole contains not less than 98.5% and not more than the equivalent of 101.5%.

**Molecular Formula:** \( \text{C}_{35}\text{H}_{38}\text{Cl}_{12}\text{N}_{8}\text{O}_{4} \)

**Characters:** White or almost white powder.

**Solubility:** practically insoluble in water, freely soluble in methylene chloride, sparingly soluble in tetrahydrofuran, very slightly soluble in alcohol.

**Storage:** store and protect from light

![Fig 12.1: Structure of Itraconazole](image)

**Drug Category**

- Antiprotozoals
- Antifungals

**Dosage Forms**

- Capsules (100 mg)
- Liquid solution
**Indications**

For the treatment of the following fungal infections in immune compromised and non-immuno compromised patients: pulmonary and extrapulmonary blastomycosis, histoplasmosis, aspergillosis and onychomycosis.

**Pharmacology**

Itraconazole is an imidazole/triazole type antifungal agent. Itraconazole is a highly selective inhibitor of fungal cytochrome P-450 sterol C-14 α-demethylation via the inhibition of the enzyme cytochrome P450 14α-demethylase. This enzyme converts lanosterol to ergosterol, and is required in fungal cell wall synthesis. The subsequent loss of normal sterols correlates with the accumulation of 14 α-methyl sterols in fungi and may be partly responsible for the fungistatic activity of fluconazole. Mammalian cell demethylation is much less sensitive to fluconazole inhibition. Itraconazole exhibits *in vitro* activity against *Cryptococcus neoformans* and *Candida spp*. Fungistatic activity has also been demonstrated in normal and immunocompromised animal models for systemic and intracranial fungal infections due to *Cryptococcus neoformans* and for systemic infections due to *Candida albicans*.

**Mechanism of Action**

Itraconazole interacts with 14-α demethylase, a cytochrome P-450 enzyme necessary to convert lanosterol to ergosterol. As ergosterol is an essential component of the fungal cell membrane, inhibition of its synthesis results in increased cellular permeability causing leakage of cellular contents. Itraconazole may also inhibit endogenous respiration, interact with membrane phospholipids, inhibit the transformation of yeasts to mycelial forms, inhibit purine uptake, and impair triglyceride and/or phospholipid biosynthesis.
Absorption

The absolute oral bioavailability of itraconazole is 55%, and is maximal when taken with a full meal.

Toxicity

No significant lethality was observed when itraconazole was administered orally to mice and rats at dosage levels of 320 mg/kg or to dogs at 200 mg/kg.

Biotransformation / Drug Metabolism

Itraconazole is extensively metabolized by the liver into a large number of metabolites, including hydroxyl itraconazole, the major metabolite. The main metabolic pathways are oxidative scission of the dioxolane ring, aliphatic oxidation at the 1-methylpropyl substituent, N-dealkylation of this 1-methylpropyl substituent, oxidative degradation of the piperazine ring and triazolone scission.

Contraindications

Co administration of terfenadine, astemizole or cisapride with Sporanox (itraconazole capsules) is contraindicated.

Concomitant administration of Sporanox with oral triazolam or with oral midazolam is contraindicated.

Sporanox should not be administered for the treatment of onychomycosis to pregnant patients or to women contemplating pregnancy.

Sporanox is contraindicated in patients who have shown hypersensitivity to the drug or its excipients. There is no information regarding cross hypersensitivity between itraconazole and other azoles antifungal agents. Caution should be used in prescribing Sporanox to patients with hypersensitivity to other azoles.
Drug Interactions

Both itraconazole and its major metabolite, hydroxyl itraconazole, are inhibitors of the cytochrome P450 3A4 enzyme system. Co administration of Itraconazole and drugs primarily metabolized by the cytochrome P450 3A4 enzyme system may result in increased plasma concentrations of the drugs that could increase or prolong both therapeutic and adverse effects. Therefore, unless otherwise specified, appropriate dosage adjustments may be necessary.

Co administration of terfenadine with Itraconazole has led to elevated plasma concentrations of terfenadine, resulting in rare instances of life-threatening cardiac dysrhythmias and one death.

Another oral azole antifungal, ketoconazole, inhibits the metabolism of astemizole, resulting in elevated plasma concentrations of astemizole and its active metabolite desmethylastemizole which may prolong QT intervals. In vitro data suggest that itraconazole, when compared to ketoconazole, has a less pronounced effect on the biotransformation system responsible for the metabolism of astemizole. Based on the chemical resemblance of itraconazole and ketoconazole, coadministration of astemizole with itraconazole is contraindicated.

Human pharmacokinetics data indicate that oral ketoconazole potently inhibits the metabolism of cisapride resulting in an eight-fold increase in the mean AUC of cisapride. Data suggest that coadministration of oral ketoconazole and cisapride can result in prolongation of the QT interval on the ECG. In vitro data suggest that itraconazole also markedly inhibits the biotransformation system mainly responsible
for the metabolism of cisapride; therefore concomitant administration of Itraconazole with cisapride is contraindicated.

Coadministration of Itraconazole with oral midazolam or triazolam has resulted in elevated plasma concentrations of the latter two drugs. This may potentiate and prolong hypnotic and sedative effects. These agents should not be used in patients treated with Itraconazole. If midazolam is administered parenterally, special precaution is required since the sedative effect may be prolonged.

When Itraconazole was coadministered with phenytoin, rifampin, or H2antagonists, reduced plasma concentrations of itraconazole were reported. The physician is advised to monitor the plasma concentrations of itraconazole when any of these drugs is taken concurrently, and to increase the dose of Itraconazole if necessary. Although no studies have been conducted, concomitant administration of Itraconazole and phenytoin may alter the metabolism of phenytoin; therefore, plasma concentrations of phenytoin should also be monitored when it is given concurrently with Itraconazole. It has been reported that Itraconazole enhances the anticoagulant effect of coumarin-like drugs. Therefore, prothrombin time should be carefully monitored in patients receiving Itraconazole and coumarin-like drugs simultaneously. Plasma concentrations of azole antifungal agents are reduced when given concurrently with isoniazid. Itraconazole plasma concentrations should be monitored when Itraconazole and isoniazid are coadministered. Severe hypoglycemia has been reported in patients concomitantly receiving azole antifungal agents and oral hypoglycemic agents. Blood glucose concentrations should be carefully monitored when Itraconazole and oral hypoglycemic agents are coadministered. Tinnitus and decreased hearing have been reported in patients concomitantly receiving Itraconazole
and quinidine. Edema has been reported in patients concomitantly receiving Itraconazole and dihydropyridine calcium channel blockers.

The results from a study in which eight HIV-infected individuals were treated with zidovudine, 8 +/- 0.4 mg/kg/day, showed that the pharmacokinetics of zidovudine were not affected during concomitant administration of Itraconazole, 100 mg b.i.d.
CLOTRIMAZOLE

**Definition:** Clotrimazole contains not less than 98.5 % and not more than the equivalent of 100.5% of 1-[(2-chlorophenyl) diphenylmethyl]-1H-imidazole.

![Structure of Clotrimazole](image)

**Fig12.2:** Structure of Clotrimazole

**Molecular Formula:** C\textsubscript{22}H\textsubscript{17}ClN\textsubscript{2}

**Characters:** A White or Pale Yellow, Crystalline Powder

**Solubility:** Practically in soluble in water, soluble in alcohol and in methylene chloride

**Melting point:** 141\textdegree\textopencurlyquote C to 150\textdegree\textopencurlyquote C

**Storage:** Protected From Light

**Drug Category:** Fungicidal.

**Pharmacological Action:** A broad spectrum antimycotic acting as fungicide.

<table>
<thead>
<tr>
<th>All dermatomycoses due to dermatophytes (e.g. <em>Trichophyton species</em>).</th>
</tr>
</thead>
<tbody>
<tr>
<td>All dermatomycoses due to yeasts (e.g. <em>Candida species</em>).</td>
</tr>
<tr>
<td>Dermatomycoses due to moulds and other fungi.</td>
</tr>
<tr>
<td>Skin diseases with secondary infection by these fungi.</td>
</tr>
</tbody>
</table>
Table 11: The range of indications is all dermatomycoses

- Mycoses of the skin and skin folds, (e.g. fungal infections of the groin, perineum, axillae, Dhobies’ or jock itch and barber’s itch.)
- Ringworm.
- Interdigital mycoses e.g. athlete's foot.
- Candida vulvitis (vulval thrush).
- Candida balanitis, (thrush of the glans penis).
- Pityriasis (Tinea) versicolor.
- Erythrasma.
- Paronychias, associated with nail mycoses, (fungal infections of the tissues adjacent to the nail of a finger or toe).

Table 12: The dermatomycoses mentioned under 1-4 include among others

Contra-Indications:

Possible hypersensitivity to clotrimazole and cetostearyl alcohol.

Dosage and Directions for Use:

Apply thinly to the affected areas 2-3 times daily and rub in. A small amount of cream or a few drops of solution is usually sufficient for an area about the size of the palm. Successful treatment demands that Canesten be applied correctly and over a sufficiently long period of time. In general, it is 3-4 weeks in the case of dermatomycoses due to dermatophytes and yeasts; in Candida vulvitis and Candida balanitis, 1-2 weeks; and approximately 2-4 weeks in Erythrasma and 1-3 weeks in Pityriasis versicolor.
Treatment of fungal infection should be continued for approximately 2 weeks after the disappearance of all symptoms despite a rapid, subjective improvement, in order to prevent relapse. It is also used in athlete's foot.

**Side Effects and Special Precautions:**

Not intended for ophthalmic use. Local reactions including skin irritation and burning may occur. Contact allergic dermatitis has been reported. In cases of systemic absorption, lower abdominal cramps, increase in urinary frequency or skin rash may occur.

**Over dosage:**

See side-effects and special precautions. In case of accidental ingestion, gastrointestinal disturbances and central nervous system depression may occur. Treatment is symptomatic and supportive.
**FLUCONAZOLE**

**Definition:** 2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)propan-2-ol.

**Molecular Formula:** $C_{13}H_{12}F_{2}N_{6}O$

**Content:** 99.0% to 101.0%

**Characters:** White or almost white, hygroscopic, crystalline powder.

**Solubility:** slightly soluble in water, freely soluble in methanol, soluble in acetone.

**Storage:** In an air tight container

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**Fig 12.3:** Structure of Fluconazole

**Generic Name:** Fluconazole

**Pronunciation:** (floo koe' na zole)
**Trade Name(s)**: Cancap, Concize, Flucan, Flucankid Tab, Flucos150, Flucos200, Flucos50, Flumed, Flutrox, Fluzide, Fluzon, Forcan, Fungal-F, Fungicon, Logican, Lucazol, Mycorest, One can, Saf-F, Syscan, Xenofun, Zocon

**Why it is prescribed**: Fluconazole, an antifungal agent, is used to treat pneumonia, meningitis, and fungal infections of the mouth, throat, liver, kidneys, heart, urinary tract, and abdomen. Fluconazole also has been used to treat vaginal infections.

**When it is to be taken**: Fluconazole is usually taken once a day. Follow the instructions on your prescription label carefully. Fluconazole must be taken regularly to be effective.

**How it should be taken**: Fluconazole comes in the form of tablets. Your prescription label tells you how much to take at each dose.

**Special Instruction**:

1. Take Fluconazole for as long as directed, even after your symptoms improve. You may have to take Fluconazole for an extended period before the infection is completely gone and periodically after that to be sure that the infection does not return.

2. Keep all appointments with your doctor and the laboratory so that your response to this drug can be evaluated.

3. If you forget to take a dose, take the missed dose as soon as you remember it. However, if you remember a missed dose at the time you are scheduled to take the next dose, take only the regularly scheduled dose. Do not take a double dose.

**Side Effects**:

1. Nausea, vomiting, abdominal pain, diarrhea, dizziness, headache, skin rash, itching.
2. Liver problems; fatigue, nausea, vomiting, yellowing of skin or eyes, dark urine, pale stools.

**Other Precautions:**

1. Before you take fluconazole, tell your doctor if you have a history of liver or kidney disease.

2. Certain medications can affect the action of Fluconazole, and Fluconazole can affect the action of other drugs.

3. Tell your doctor what prescription and nonprescription drugs you are taking, especially anticoagulants, cyclosporine, phenytoin, rifampin, and oral medication for diabetes.

4. Women who are pregnant or breast-feeding should inform their doctors.

5. Do not allow anyone else to take your medication.

**Storage Conditions:** Keep this medication in the container it came in, tightly closed, and out of the reach of children. Store it at room temperature. (IP, 2007; BP, 2005; USP 2000)
**TERBINAFINE HCL**

*Fig 13: Structure of Terbinafine Hcl*

**Uses:**

Terbinafine is used to treat certain types of fungal infections (e.g., fingernail or toenail). It works by stopping the growth of fungus. This medication belongs to a class of drugs known as antifungal.

**How to Use:**

Take this medication by mouth, usually once a day, or as directed by your doctor. It may be taken with or without food. Dosage and duration of therapy is based on your medical condition and response to therapy. It may take several months after completion of treatment to see the full benefit of this drug. It takes time for your new healthy nails to grow out and replace the infected nails. Continue to take this medication until the full prescribed amount is finished. Stopping the medication too early may allow the fungus to continue to grow, which may result in a relapse of the infection. Inform your doctor if your condition persists or worsens.
Side Effects:

Diarrhoea, stomach upset, temporary change or loss of taste, or tiredness, fever, chills, and persistent sore throat), easy bruising/bleeding, and vision changes. This drug rarely has caused very serious (possibly fatal) liver disease, persistent nausea, loss of appetite, severe stomach/abdominal pain, dark urine, vomiting, yellowing of eyes or skin. A very serious allergic reaction to this drug is unlikely, but seeks immediate medical attention if it occurs. Symptoms of a serious allergic reaction may include: rash, itching, swelling, severe dizziness, trouble breathing.

Drug Interactions:

Rifampin reduces terbinafine blood concentrations, potentially reducing the efficacy of terbinafine, and cimetidine (Tagamet) may increase terbinafine blood levels. The latter effect would not be expected to lead to problems.

Pregnancy:

Studies in animals using large dosages of terbinafine have not demonstrated toxic effects on the fetus; however, there have not been conclusive studies in humans. Since fungal infections of the skin and nails usually are not a serious problem, the manufacturer of terbinafine does not recommend therapy during pregnancy.
POLYMER PROFILE

CARBOMER

Synonyms

Acrypol; Acritamer; acrylic acid polymer; carbomera; Carbopol; carboxy polymethylene; polyacrylic acid; carboxyvinyl polymer; Pemulen; Tego Carbomer

Fig 14: Structure of Carbomer

Typical Properties

Acidity/alkalinity

\[ \text{pH} = 2.5 - 4.0 \text{ for a } 0.2\% \text{ w/v aqueous dispersion; } \]

Density (bulk)

0.2 g/cm\(^3\) (powder); 0.4 g/cm\(^3\) (granular).

Density (tapped)

0.3 g/cm\(^3\) (powder); 0.4 g/cm\(^3\) (granular).

Dissociation constant pKa

6.0–0.5

Glass transition temperature

100–105.8°C

Melting point

Decomposition occurs within 30 minutes at 260.8°C.

Moisture content

typical water content is up to 2% w/w.

Specific gravity

1.41

Solubility

Swellable in water and glycerin

Viscosity, (dynamic):

Carbomers disperse in water to form acidic colloidal dispersions that, when neutralized, produce highly viscous gels. Carbomer powders should first be dispersed
into vigorously stirred water, taking care to avoid the formation of indispersible agglomerates, then neutralized by the addition of a base. These carbomers wet quickly yet hydrate slowly, while possessing a lower UN neutralized dispersion viscosity. Agents that may be used to neutralize carbomer polymers include amino acids, potassium hydroxide, sodium bicarbonate, sodium hydroxide, and organic amines such as triethanolamine. Aqueous gels are more viscous at pH 6–11. The viscosity is considerably reduced at pH values less than 3 or greater than 12, or in the presence of strong electrolytes.

**Incompatibilities**

Carbomers are discolored by resorcinol and are incompatible with phenol, cationic polymers, strong acids, and high levels of electrolytes. Certain antimicrobial adjuvant should also be avoided or used at low levels. Carbomers also form pH-dependent complexes with certain polymeric excipients. Adjustment of pH and/or solubility parameter can also work in this situation.

**Applications in Pharmaceutical Formulation**

Carbomers are used in liquid or semisolid pharmaceutical formulations as rheology modifiers. Formulations include creams, gels, lotions and ointments for use in ophthalmic, rectal, topical and vaginal preparations. Carbomer having low residuals of ethyl acetate, such as Carbopol 971P NF or Carbopol 974P NF, may be used in oral preparations, in suspensions, capsules or tablets In tablet formulations, carbomers are used as controlled release agents and/or as binders. In contrast to linear polymers, higher viscosity does not result in slower drug release with carbomers. Lightly crosslinked carbomers (lower viscosity) are generally more efficient in controlling drug release than highly crosslinked carbomers (higher viscosity). In wet granulation processes, water, solvents or their mixtures can be used as the granulating fluid. The
tackiness of the wet mass may be reduced by including talc in the formulation or by adding certain cationic species to the granulating fluid. However, the presence of cationic salts may accelerate drug release rates and reduce bioadhesive properties. Carbomer polymers have also been investigated in the preparation of sustained-release matrix beads, as enzyme inhibitors of intestinal proteases in peptide-containing dosage forms, as a bioadhesive for a cervical patch and for intra nasally administered microspheres, in magnetic granules for site-specific drug delivery to the esophagus, and in oral mucoadhesive controlled drug delivery systems Carbomers copolymers are also employed as emulsifying agents in the preparation of oil-in-water emulsions for external administration. Carbomer 951 has been investigated as a viscosity-increasing aid in the preparation of multiple emulsion microspheres Carbomers are also used in cosmetics. Therapeutically, carbomer formulations have proved efficacious in improving symptoms of moderate-to-severe dry eye syndrome.
CARBOXY METHYLCELLULOSE SODIUM

Synonyms

Akucell; Aqualon CMC; Aquasorb; Blanose; Carbose D; carmellosum natricum; Cel-O-Brandt; cellulose gum; Cethylose; CMC Sodium; E466; Finnfix; Glykocellan; Nymcel ZSB; SCMC; sodium carboxy methylcellulose; sodium cellulose glycolate; Sunrose; Tylose CB; Tylose MGA; Walocel C; Xylo-Mucine.

Fig 15: Structure of CMC

Typical Properties

Density (bulk) 0.52 g/cm³
Density (tapped) 0.78 g/cm³
Dissociation constant pKa 4.30
Melting point Browns at 2278°C, and chars at 2528°C.
Moisture content Typically contains less than 10% water.
Solubility Practically insoluble in acetone, ethanol
Viscosity 5–2000 mPa s (5– 2000 Cps) may be obtained.
Applications in Pharmaceutical Formulation:

Carboxymethylcellulose sodium is widely used in oral and topical pharmaceutical formulations, primarily for its viscosity-increasing properties. Viscous aqueous solutions are used to suspend powders intended for either topical application or oral and parenteral administration. Carboxymethylcellulose sodium may also be used as a tablet binder and disintegrant, and to stabilize emulsions. Higher concentrations, usually 3–6%, of the medium-viscosity grade are used to produce gels that can be used as the base for applications and pastes; glycols are often included in such gels to prevent them drying out. Carboxymethylcellulose sodium is also used in self-adhesive wound care, and dermatological patches as a mucoadhesive and to absorb wound exudates or transepidermal water and sweat. This mucoadhesive property is used in products designed to prevent post-surgical tissue adhesions; and to localize and modify the release kinetics of active ingredients applied to mucous membranes; and for bone repair. Encapsulation with carboxymethylcellulose sodium can affect drug protection and delivery. There have also been reports of its use as cyto-protective agent. Carboxymethylcellulose sodium is also used in cosmetics, toiletries, surgical prosthetics, and incontinence, personal hygiene, and food products.

Incompatibilities

Carboxymethylcellulose sodium is incompatible with strongly acidic solutions and with the soluble salts of iron and some other metals, such as aluminum, mercury, and zinc. It is also incompatible with xanthan gum. Precipitation may occur at pH < 2, and also when it is mixed with ethanol (95%). Carboxymethylcellulose sodium forms
complex coacervates with gelatin and pectin. It also forms a complex with collagen and is capable of precipitating certain positively charged proteins.

**GUAR GUM**

**Synonyms**

E412; Galactosol; guar flour; guar galactomannanum; jaguar gum; Meyprogat; Meyprodo; Meyprofin

![Structure of Guar gum](image)

**Fig 16: Structure of Guar gum**

**Typical Properties**

- **Acidity/alkalinity pH**: 5.0–7.0 (1% w/v aqueous dispersion)
- **Density**: 1.492 g/cm$^3$
- **Colour**: white to yellowish white
- **Odour**: odorless or nearly odorless
- **Taste**: bland taste
- **Texture**: **powder**
- **Solubility**: Practically insoluble in organic solvents. In cold or hot water,
- **Viscosity**: (dynamic) 4.86 Pa s (4860 Cps) for a 1% w/v soln.
Applications in Pharmaceutical Formulation:

Guar gum is a galactomannan, commonly used in cosmetics, food products, and pharmaceutical formulations. It has also been investigated in the preparation of sustained-release matrix tablets in the place of cellulose derivatives such as methylcellulose. In pharmaceuticals; guar gum is used in solid-dosage forms as a binder and disintegrant, in oral and topical products as a suspending, thickening, and stabilizing agent; and also as a controlled-release carrier. Guar gum has also been examined for use in colonic drug delivery. Guar-gum-based three-layer matrix tablets have been used experimentally in oral controlled-release formulations. Therapeutically, guar gum has been used as part of the diet of patients with diabetes mellitus. It has also been used as an appetite suppressant, although its use for this purpose, in tablet form, is now banned in the UK.

Incompatibilities

Guar gum is compatible with most other plant hydrocolloids such as tragacanth. It is incompatible with acetone, ethanol (95%), tannins, strong acids, and alkalis. Borate ions, if present in the dispersing water, will prevent the hydration of guar gum. However, the addition of borate ions to hydrated guar gum produces cohesive structural gels and further hydration is then prevented. The gel formed can be liquefied by reducing the pH to below 7 or by heating.
POLOXAMER

Synonyms

Lutrol; Monolan; Pluronic; poloxalkol; poloxamera; polyethylene–propylene glycol copolymer; polyoxyethylene–polyoxypropylene copolymer; Supronic; Synperonic.

STRUCTURE

Fig 17: structure of poloxamer

Typical Properties

Acidity/alkalinity: pH = 5.0–7.4 for a 2.5% w/v aqueous solution.

Density: 1.06 g/cm$^3$ at 258°C

Flowability: Solid poloxamers are free flowing.

HLB value: 0.5–30; 29 for poloxamer 188.

Melting point: 52–578°C for poloxamer 188.

Moisture content: Poloxamers generally contain less than 0.5%.

Solubility: Solubility varies according to the poloxamer type.

Surface tension: 19.8mN/m (19.8 dynes/cm)

Viscosity (dynamic): 1000 mPa s (1000 Cps) as a melt at 778°C
<table>
<thead>
<tr>
<th>Poloxamer grades</th>
<th>Physical form</th>
</tr>
</thead>
<tbody>
<tr>
<td>124</td>
<td>Liquid</td>
</tr>
<tr>
<td>188</td>
<td>Solid</td>
</tr>
<tr>
<td>237</td>
<td>Solid</td>
</tr>
<tr>
<td>338</td>
<td>Solid</td>
</tr>
<tr>
<td>407</td>
<td>Solid</td>
</tr>
</tbody>
</table>

**Table 13:** properties of polaxamer grade

<table>
<thead>
<tr>
<th>Type</th>
<th>Ethanol 95%</th>
<th>Propan-2-ol</th>
<th>Propylene glycol</th>
<th>water</th>
<th>xylene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poloxamer 124</td>
<td>Freely soluble</td>
<td>Freely soluble</td>
<td>Freely soluble</td>
<td>Freely soluble</td>
<td>Freely soluble</td>
</tr>
<tr>
<td>Poloxamer 124</td>
<td>Freely soluble</td>
<td>_</td>
<td>_</td>
<td>Freely soluble</td>
<td>_</td>
</tr>
<tr>
<td>Poloxamer 124</td>
<td>Freely soluble</td>
<td>Sparingly soluble</td>
<td>_</td>
<td>Freely soluble</td>
<td>Sparingly soluble</td>
</tr>
<tr>
<td>Poloxamer 124</td>
<td>Freely soluble</td>
<td>_</td>
<td>Sparingly soluble</td>
<td>Freely soluble</td>
<td>_</td>
</tr>
<tr>
<td>Poloxamer 124</td>
<td>Freely soluble</td>
<td>Freely soluble</td>
<td>Sparingly soluble</td>
<td>Freely soluble</td>
<td>_</td>
</tr>
</tbody>
</table>

**Table 14:** solubility at 20°c for varies types of poloxamer in different solvent properties of polaxamer grade

**Applications in Pharmaceutical Formulation**
Poloxamers are nonionic polyoxyethylene–polyoxypropylene copolymers used primarily in pharmaceutical formulations as emulsifying or solubilizing agents. The polyoxyethylene segment is hydrophilic while the polyoxypropylene segment is hydrophobic. All of the poloxamers are chemically similar in composition, differing only in the relative amounts of propylene and ethylene oxides added during manufacture. Their physical and surface-active properties vary over a wide range and a number of different types are commercially available; Poloxamers are used as emulsifying agents in intravenous fat emulsions, and as solubilizing and stabilizing agents to maintain the clarity of elixirs and syrups. Poloxamers may also be used as wetting agents; in ointments, suppository bases, and gels; and as tablet binders and coatings. Poloxamer 188 has also been used as an emulsifying agent for fluorocarbons used as artificial blood substitutes, and in the preparation of solid-dispersion systems. More recently, poloxamers have found use in drug-delivery systems. Therapeutically, poloxamer 188 is administered orally as a wetting agent and stool lubricant in the treatment of constipation; it is usually used in combination with a laxative such as danthron. Poloxamers may also be used therapeutically as wetting agents in eye-drop formulations, in the treatment of kidney stones, and as skin-wound cleansers. Poloxamer 338 and 407 are used in solutions.

<table>
<thead>
<tr>
<th>Table 15: Uses of poloxamer.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use</td>
</tr>
<tr>
<td>Fat emulsifier</td>
</tr>
<tr>
<td>Flavor solubilizer</td>
</tr>
<tr>
<td>Fluorocarbon emulsifier</td>
</tr>
<tr>
<td>Gelling agent</td>
</tr>
<tr>
<td>Spreading agent</td>
</tr>
<tr>
<td>Stabilizing agent</td>
</tr>
<tr>
<td>Suppository base</td>
</tr>
<tr>
<td>Tablet coating</td>
</tr>
<tr>
<td>Tablet excipient</td>
</tr>
<tr>
<td>Wetting agent</td>
</tr>
</tbody>
</table>

Table 15: use of poloxamer grade
Incompatibilities

Depending on the relative concentrations, poloxamer 188 is incompatible with phenols and parabens.

XANTHAN GUM

Synonyms

Corn sugar gum; E415; Grindsted; Keldent; Keltrol; polysaccharide B-1459; Rhodicare S; Rhodigel; Vanzan NF; xanthani gummi; Xantural.

![Structure of Xanthan gum](image)

**Fig 18:** Structure of Xanthan gum

**Typical Properties**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidity/alkalinity pH</td>
<td>6.0–8.0 for a 1% w/v aqueous solution.</td>
</tr>
<tr>
<td>Freezing point</td>
<td>08°C for a 1% w/v aqueous solution.</td>
</tr>
<tr>
<td>Heat of combustion</td>
<td>4.6 J/g (3.5 cal/g)</td>
</tr>
<tr>
<td>Melting point</td>
<td>Chars at 270°C</td>
</tr>
<tr>
<td>Refractive index</td>
<td>n D 20 = 1.333 (1% w/v aqueous solution).</td>
</tr>
</tbody>
</table>
**Solubility**  
Practically insoluble in ethanol and ether; soluble in Cold or warm water.

**Specific gravity**  
1.600 at 25°C

**Viscosity (dynamic)**  
1200–1600 mPa s (1200–1600 Cps) for a 1% w/v aqueous solution at 25.8°C.

---

**Applications in Pharmaceutical Formulation**

Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending and stabilizing agent. It is also used as a thickening and emulsifying agent. It is nontoxic, compatible with most other pharmaceutical ingredients, and has good stability and viscosity properties over a wide pH and temperature range. Xanthan gum gels show pseudo plastic behavior, the shear thinning being directly proportional to the shear rate. The viscosity returns to normal immediately on release of shear stress. Xanthan gum has been used as a suspending agent for conventional dry and sustained-release suspensions. When xanthan gum is mixed with certain inorganic suspending agents, such as magnesium aluminum silicate, or organic gums, synergistic rheological effects occur. In general, mixtures of xanthan gum and magnesium aluminum silicate in ratios between 1: 2 and 1: 9 produce the optimum properties. Similarly, optimum synergistic effects are obtained with xanthan gum: guar gum ratios between 3: 7 and 1: 9. Although primarily used as a suspending agent, xanthan gum has also been used to prepare sustained-release matrix tablets. Controlled-release tablets of diltiazem hydrochloride prepared using xanthan gum have been reported to sustain the drug release in a
predictable manner, and the drug release profiles of these tablets were not affected by pH and agitation rate. Xanthan gum has also been used to produce directly compressed matrices that display a high degree of swelling due to water uptake, and a small amount of erosion due to polymer relaxation. It has also been used in combination with chitosan, guar gum and sodium alginate to prepare sustained-release matrix tablets.

Xanthan gum has been used as a binder, and in combination with Konjac glucomannan is used as an excipient for controlled colonic drug delivery. Xanthan gum with boswellia (3 : 1) and guar gum (10 : 20) have shown the best release profiles for the colon-specific compression coated systems of 5-fluorouracil for the treatment of colorectal cancer. Xanthan gum has also been used with guar gum for the development of a floating drug delivery system. It has also has derivatized to sodium carboxymethyl xanthan gum and crosslinked with aluminum ions to prepare microparticles, as a carrier for protein delivery. Xanthan gum has been incorporated in an ophthalmic liquid dosage form, which interacts with mucin, thereby helping in the prolonged retention of the dosage form in the precorneal area. When added to liquid ophthalmic, xanthan gum delays the release of active substances, increasing the therapeutic activity of the pharmaceutical formulations. Xanthan gum can be used to increase the bioadhesive strength in vaginal formulations. Xanthan gum alone or with carbopol 974P has been used as a mucoadhesive controlled-release excipient for buccal drug delivery. Modified xanthan films have been used as a matrix system for transdermal delivery of atenolol. Xanthan gum has also been used as a gelling agent for topical formulations incorporating solid lipid nanoparticles of vitamin A or microemulsion of ibuprofen. A combined polymer system consisting of xanthan gum, carboxy methylcellulose and a polyvinyl pyrolidone backboned polymer has been
used for relieving the symptoms of xerostomia. Xanthan gum can also be used as an excipient for spray-drying and freeze-drying processes for better results. It has been successfully used alone or in combination with agar for microbial culture media. Xanthan gum is also used as a hydrocolloid in the food industry, and in cosmetics it has been used as a thickening agent in shampoo. Polyphosphate with xanthum gum in soft drinks is suggested to be effective at reducing erosion of enamel.

**Incompatibilities**

Xanthan gum is an anionic material and is not usually compatible with cationic surfactants, polymers, or preservatives, as precipitation occurs. Anionic and amphoteric surfactants at concentrations above 15% w/v cause precipitation of xanthan gum from a solution. Under highly alkaline conditions, polyvalent metal ions such as calcium cause gelation or precipitation; this may be inhibited by the addition of a glucoheptonate sequestrant. The presence of low levels of borates (<300 ppm) can also cause gelation. This may be avoided by increasing the boron ion concentration or by lowering the pH of a formulation to less than pH 5. The addition of ethylene glycol, sorbitol, or mannitol may also prevent this gelation. Xanthan gum is compatible with most synthetic and natural viscosity-increasing agents, many strong mineral acids, and up to 30% inorganic salts. If it is to be combined with cellulose derivatives, then xanthan gum free of cellulose should be used to prevent depolymerization of the cellulose derivative. Xanthan gum solutions are stable in the presence of up to 60% water-miscible organic solvents such as acetone, methanol, ethanol, or propan-2-ol. However, above this concentration precipitation or gelation occurs.
HYDROXY PROPYL METHYL CELLULOSE

**Synonyms**
Methocel, Benecel, HPMC, Metolose.

**Chemical name**
Propylene glycol ether of methyl cellulose.

**Molecular Weight**
13000-208000

![Fig 19: structure of HPMC](image)

**Description**
It is an odorless and tasteless, white or creamy-white colored fibrous or granular powder.

**Solubility**
Soluble in cold water, forming a viscous colloidal solution, practically insoluble in matrix of ethanol and dichloromethane, mixtures of alcohol and water.

**Incompatibilities**
Incompatible with some oxidizing agent.

**Functional Category**
Coating agent, film former, rate controlling polymer for sustained release, stabilizing agent, suspending agent, viscosity increasing agent.

**Applications in pharmaceutical formulation**
Coating agent, film former, rate controlling polymer for sustained release, stabilizing agent, suspending agent, viscosity increasing agent.

**Stability and storage conditions**
It is a stable material although it is hygroscopic after drying. It should be stored in a well-closed container, in a cool and dry place.
SODIUM ALGINATE

Synonyms: Alginic acid, sodium salt; ammonium polymannuronate; E404; Keltose.

![Fig 20: Structure of Sodium Alginate](image)

Chemical Name
Ammonium alginate

Empirical Formula and Molecular Weight
(C6H11NO6) n 193.16 (calculated) 217 (actual, average)
Ammonium alginate is the ammonium salt of alginic acid

Description
Ammonium alginate occurs as white to yellowish brown filamentous, grainy, granular, or powdered forms.

Typical Properties
Moisture content Not more than 15% at 105.8°C for 4 hours.
Solubility Dissolves slowly in water to form a viscous solution; insoluble in ethanol and in ether.


Applications in Pharmaceutical Formulation
Ammonium alginate is widely used in foods as a stabilizer, thickener and emulsifier. It is also used in pharmaceutical preparations as a color-diluents, emulsifier, film-former, and humectants.

**Stability and Storage Conditions**

Ammonium alginate is a hygroscopic material, although it is stable, if stored at low relative humidities and cool temperatures.

**Incompatibilities**

Incompatible with oxidizing agents and strong acids and alkalis
GELLAN GUM

Definition:

Gellan gum is a high molecular weight polysaccharide gum produced by a pure culture fermentation of a carbohydrate by *Pseudomonas elodea*, purified by recovery with isopropyl alcohol, dried, and milled. The high molecular weight polysaccharide is principally composed of a tetra saccharine repeating unit of one ramose, one glucuronic acid, and two glucose units, and is substituted with acyl (glyceryl and acetyl) groups as the O-glycosidically-linked esters. The glucuronic acid is neutralized to a mixed potassium, sodium, calcium, and magnesium salt. It usually contains a small amount of nitrogen containing compounds resulting from the fermentation procedures.

![Structure of Gellan Gum](image)

**Fig 21:** Structure of Gellan Gum

**Formula Weight:** Approximately 500,000

**Description:** Off-white powder

**Uses:** Thickening agent, gelling agent, stabilizer

**Identification**

**Solubility:** Soluble in water, forming a viscous solution; insoluble in ethanol.
**Gel test with calcium ion:** Add 1.0 g of the sample to 99 ml of water, and stir for about 2 h,

Motorized stirrer having a propeller-type stirring blade. Draw a small amount of this solution into a wide bore pipette and transfer into a 10% solution of calcium chloride. A tough worm-like gel will be formed immediately.

**Gel test with sodium ion:** Add 1.0 g of the sample to 99 ml of water, and stir for about 2 h, motorized stirrer having a propeller-type stirring blade. Add 0.50 g of sodium chloride, heat to 80° with stirring, and hold at 80° for 1 min. Allow the solution to cool to room temperature. A firm gel is formed.

**PURITY:**

- **Loss On Drying:** not more than 15% (105, 21/2 h)
- **Nitrogen:** not more than 3%
- **Isopropyl alcohol:** not more than 750mg/kg

**Microbiological criteria:** Total plate count: Not more than 10,000 colonies per gram

- **E. coli:** Negative by test
- **Salmonella:** Negative by test
- **Yeast and moulds:** Not more than 400 colonies per gram.

**Advantages of Gelrite Gellan Gum**

- Gelrite gum may be used at approximately half the use level of agar.
- Gelrite, produced by a tightly-controlled fermentation process, it has consistent Product quality. gelrite is unaffected by the vagaries of natural conditions
- Gelrite gels are remarkably clear in comparison to those formed with agar.
- Gels prepared with gelrite set faster than those made with agar. in microbiological
• Gels prepared with gelrite are stable at high temperatures. in microbiological media,
  This supports incubation required by hemophilic microorganisms.
• Gelrite contains no contaminating matters (e.g., phenol compounds) as those found
  In agar that are toxic to certain sensitive organisms.
• Gelrite gum disperses and hydrates easily in either hot or cold deionized water, forming viscous solutions in cold distilled water.
• Gelrite in the presence of soluble salts. gelrite can be used to provide high gel strength at low
• Gelrite concentrations (normally at approximately half the concentration required for agar.
• Gelrite at high temperatures, the low viscosity of gelrite solutions facilitates pipetting, pumping, and pouring; upon cooling, gelrite solutions gel quickly and uniformly.
• Gelrite is able to withstand normal autoclaving conditions.
• Gelrite is generally resistant to enzymatic degradation.
• Gelrite itself is chemically inert to most biological growth media additives.

(RPS 21st edition; www.google.com)

Objective of study
The present therapy adopted by physicians for the treatment of oral thrush includes the systemic administration and oral solution of antifungal agents. A concern in these formulations involves systemic adverse effects and also less concentration of drug at the site of infection. Hence an attention has recently been focused on topical delivery of antifungal agents which is the most widely accepted approach.

Objective of the present study is to prolong the delivery of the active drug in the oral cavity using a suitable carrier such as in situ gels which can effectively deliver the drug for an extended duration of time hence not only reduce the systemic side effects but also improve the therapeutic efficacy, patient compliance. Local drug delivery systems are better suitable for antifungal drugs particularly for oral thrush.

Over the past two decades, extensive research has been performed in the design of polymeric drug delivery systems. Among them, new series of thermosensitive, ion induced and pH sensitive in situ gel systems are potential carriers of antifungal drugs for oral thrush. These systems are made of biodegradable polymers, which can be injected via a syringe into the infected area where the solution translate into gel depot\(^4,5\).

Smart polymeric systems represent promising means of delivering the drugs; these polymers undergo sol-gel transition in accordance with the biological stimuli like pH change, temperature modulation and ion exchange.

The purpose of the present investigation is to develop the in situ gel formulations containing the antifungal agents such as Clotrimazole, Fluconazole, Itraconazole, ciclopriox olamine and PVP iodine for treatment of Oral Thrush.
Specific objective of the present investigation are as follows.

1. To develop the ion induced, pH induced, temperature reverse *in situ* gel formulation containing antifungal agents.
2. To evaluate the optimized formulation for the gelation time, gelation capacity, viscosity, gel strength, mucoadhesive force, spreadability, gelation temperature (temperature reverse system) and *in vitro* drug release.
3. Evaluation of optimized in situ gel formulations for various parameters such as FTIR, DSC and XRD.
4. To evaluate the anti fungal activity against *Candida albicans*
5. To test the usefulness of these drug-loaded formulation (*in vivo*)
Figure 10: Advantage of in situ gel
## MATERIALS

**Table 16**

**List of Ingredients**

<table>
<thead>
<tr>
<th>Chemicals</th>
<th>Manufactured by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clotrimazole</td>
<td>Fourt’s India, Chennai</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Fourt’s India, Chennai</td>
</tr>
<tr>
<td>Ciclopriox Olamine</td>
<td>Glenmark pharmaceuticals Ltd (Mumbai)</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Spansules pharmatech (p) Ltd. India</td>
</tr>
<tr>
<td>PVP Iodine</td>
<td>Bliss chemicals &amp; pharmaceuticals India Ltd. (Thane) S</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>Systopic Laboratories, New Delhi</td>
</tr>
<tr>
<td>Sodium Alginate</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>HPMC K15</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>Guar Gum</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>Gellan Gum</td>
<td>Priya Multinational, Mumbai</td>
</tr>
<tr>
<td>Xanthan Gum</td>
<td>Pharmaceutical Pvt Ltd, Navi Mumbai</td>
</tr>
<tr>
<td>HPMC 100 Cps</td>
<td>Hetro Labs Limited, Andra Pradesh</td>
</tr>
<tr>
<td>Poloxamer 188</td>
<td>Pharmaceutical Pvt Ltd, Navi Mumbai</td>
</tr>
<tr>
<td>Sodium CMC</td>
<td>Wilson Laboratories, Mumbai-2</td>
</tr>
<tr>
<td>Carbopol 934</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>DMSO</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>N- methyl 2- pyrrolidone</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>Methyl prednisolone</td>
<td>Neiss Labs Ltd, India</td>
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<td>Item</td>
<td>Supplier</td>
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<td>-----------------------------------------</td>
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<tr>
<td>Gentamycin sulphate injection</td>
<td>M/S Pharmaceutical and Industrial Laboratories, India</td>
</tr>
<tr>
<td>Normal saline</td>
<td>United Surgical Industries, India</td>
</tr>
<tr>
<td>Candida albican</td>
<td>Bio Genic Laboratories, Hubli, Karnataka</td>
</tr>
<tr>
<td>Potato Dextrose Agar (PDA)</td>
<td>Merk, Mumbai</td>
</tr>
<tr>
<td>Tetracyclin</td>
<td>Lupin Pharmaceutical, India</td>
</tr>
<tr>
<td>HPMC 100Cps</td>
<td>Fourt’s, India</td>
</tr>
</tbody>
</table>
### Equipment and Animals Used

**Table 17**

List of Instruments and Equipment used

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTIR Spectra</td>
<td>FTIR-8400S Shimadzu USA</td>
</tr>
<tr>
<td>DSC Spectra</td>
<td>DSC 60, having TA60 software, Shimadzu, Japan</td>
</tr>
<tr>
<td>XRD</td>
<td>Seifert 3003 TT</td>
</tr>
<tr>
<td>Spreadability apparatus</td>
<td>(Assemble)</td>
</tr>
<tr>
<td>Brookfield DV-II+ Pro Digital Viscometer</td>
<td>USA</td>
</tr>
<tr>
<td>Olympus 70 G Camera</td>
<td>Japan</td>
</tr>
<tr>
<td>Magnetic stirrer</td>
<td>H. L. Scientific Industries - India</td>
</tr>
<tr>
<td>Diffusion cell</td>
<td>(Assemble)</td>
</tr>
<tr>
<td>Gel strength apparatus</td>
<td>(Assemble)</td>
</tr>
<tr>
<td>Bioadhesive strength apparatus</td>
<td>(Assemble)</td>
</tr>
<tr>
<td>1700 UV-VIS spectrophotometer.</td>
<td>Shimadzu USA</td>
</tr>
</tbody>
</table>

**Animals**

Mice

**Organism**

*Candida albicans*