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Article on Formulation and Evaluation of Itraconazole Anti-Fungal Emulsion

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ABSTRACT: *Fungal infections have become a serious and growing health concern worldwide, particularly among immune compromised individuals such as HIV/AIDS patients, diabetics, and those undergoing cancer chemotherapy. Itraconazole, a broad-spectrum triazole antifungal agent, is widely used for the treatment of superficial and systemic fungal infections caused by Candida species, Aspergillus species, and various dermatophytes. However, its clinical utility is significantly limited by its extremely poor aqueous solubility and inconsistent oral bioavailability, as it belongs to BCS Class II category of drugs.*

This study focuses on the formulation and evaluation of an oil-in-water (o/w) emulsion of itraconazole for oral administration, using Indian Pharmacopoeia (IP) grade excipients. The formulation was developed using Castor Oil IP as the oil phase, Acacia IP and Polysorbate 80 as the emulsifying agents, and Glycerin IP as a viscosity enhancing stabilizer to prevent phase separation. Three formulations (F1, F2, F3) were prepared by varying the concentrations of Acacia and Glycerin and evaluated for various physicochemical parameters.

The prepared emulsions were evaluated for organoleptic properties, pH, viscosity, homogeneity, droplet size, creaming index, drug content, and stability studies. The results showed that the formulation produced a stable, uniform, and patient-acceptable emulsion with improved drug solubilization and promising drug release profile. The liquid dosage form makes it particularly suitable for pediatric, geriatric, and dysphagic patients who face difficulties swallowing conventional capsule formulations.

KEYWORDS: *Itraconazole, Antifungal Emulsion, BCS Class II, Oil-in-Water Emulsion, Castor Oil, Acacia, Polysorbate 80, Indian Pharmacopoeia, Oral Bioavailability, Candida*

I. INTRODUCTION

The word "emulsion" is derived from the Latin word *emulgere*, meaning "to milk out," which reflects its nature as a two-phase system where one liquid is dispersed in another immiscible liquid in the form of fine droplets.

Fungal infections, medically known as mycoses, are caused by pathogenic fungi and have become a major public health problem across the globe. These infections range from mild superficial skin conditions to severe, life-threatening systemic diseases. The growing population of immunocompromised patients—including those with HIV/AIDS, diabetes mellitus, organ transplants, and malignancies—has contributed to a dramatic rise in the incidence of both superficial and invasive fungal infections in recent decades.

Itraconazole is a synthetic triazole antifungal agent with a broad spectrum of activity against a wide variety of fungi including *Candida* species, *Aspergillus* species, *Cryptococcus neoformans*, dermatophytes, and many other pathogenic fungi. It acts by inhibiting the enzyme 14- α demethylase, which is essential for the biosynthesis of ergosterol—the primary structural component of the fungal cell membrane. Depletion of ergosterol disrupts the integrity and function of the fungal cell membrane, ultimately leading to fungal cell death.

Despite its impressive antifungal spectrum, itraconazole is classified as a BCS Class II drug—meaning it has high permeability but very low aqueous solubility (less than 1 $\mu\text{g/mL}$ at physiological pH). This poor solubility severely limits its dissolution and absorption from conventional solid dosage forms like capsules and tablets. The oral bioavailability of itraconazole from capsule formulations is highly variable and significantly influenced by food intake, gastric pH, and patient-specific factors, leading to unpredictable therapeutic outcomes.

The formulation of itraconazole as an oral oil-in-water emulsion offers a scientifically sound and practically viable solution to these challenges. In an emulsion, the drug is already pre-dissolved in the oil phase, eliminating the slow and often incomplete dissolution step. The fine oil droplets, when ingested, mimic the physiological effect of a fatty meal and promote lymphatic absorption of the drug, effectively bypassing hepatic first-pass metabolism and significantly improving bioavailability.

Additionally, the liquid dosage form of an emulsion offers important advantages for special patient populations.

Pediatric patients who cannot swallow capsules, elderly patients with swallowing difficulties, and critically ill patients who require oral antifungal therapy all stand to benefit greatly from a well-formulated itraconazole emulsion. The ability to accurately measure and administer weight-based doses further enhances its clinical utility, particularly in children.

Thus, the present work is aimed at formulating and evaluating a stable, phase-separation-resistant oral oil-in-water emulsion of itraconazole using minimal IP-grade excipients, with the goal of improving drug delivery, patient acceptability, and therapeutic outcomes in fungal infections.



FigNo:1

II. TYPES OF FUNGAL INFECTIONS

- Superficial Mycoses
- Cutaneous Mycoses (Dermatophytosis)
- Subcutaneous Mycoses
- Systemic/Invasive Mycoses
- Opportunistic Mycoses
- Oral Candidiasis
- Onychomycosis (Nail Fungal Infection)

1) Superficial Mycoses:

These infections affect only the outermost layers of the skin, hair, and nails without penetrating the viable tissue. They cause mainly cosmetic problems and mild discomfort. Examples include tinea versicolor caused by *Malassezia furfur* and piedra caused by *Trichosporon* species.

2) Cutaneous Mycoses (Dermatophytosis):

These infections involve the keratinized layers of the skin, hair, and nails. They are caused by dermatophytes—fungi belonging to the genera *Trichophyton*, *Microsporum*, and *Epidermophyton*. Common conditions include tinea corporis (ringworm of the body), tinea capitis (scalp ringworm), tinea pedis (athlete's foot), tinea cruris (jockitch), and tinea unguium (nail infection).

3) Subcutaneous Mycoses:

These infections affect the skin, subcutaneous tissue, and sometimes bone. They usually follow traumatic implantation of fungal material from the soil or plant matter. Examples include sporotrichosis and chromoblastomycosis. They are more common in agricultural workers in tropical countries.

4) Systemic/Invasive Mycoses:

These are the most serious fungal infections, involving the internal organs and blood. They are caused by highly virulent fungi such as *Histoplasma capsulatum*, *Blastomyces dermatitidis*, and *Coccidioides immitis*, and can affect even healthy individuals through inhalation of fungal spores from the environment.

5) Opportunistic Mycoses:

These infections are caused by normally harmless fungi that become pathogenic when the host immune system is weakened. The most important examples are invasive candidiasis, invasive aspergillosis, cryptococcal meningitis, and mucormycosis. These carry very high mortality rates in immunocompromised patients.

6) *Oral Candidiasis (Thrush):*

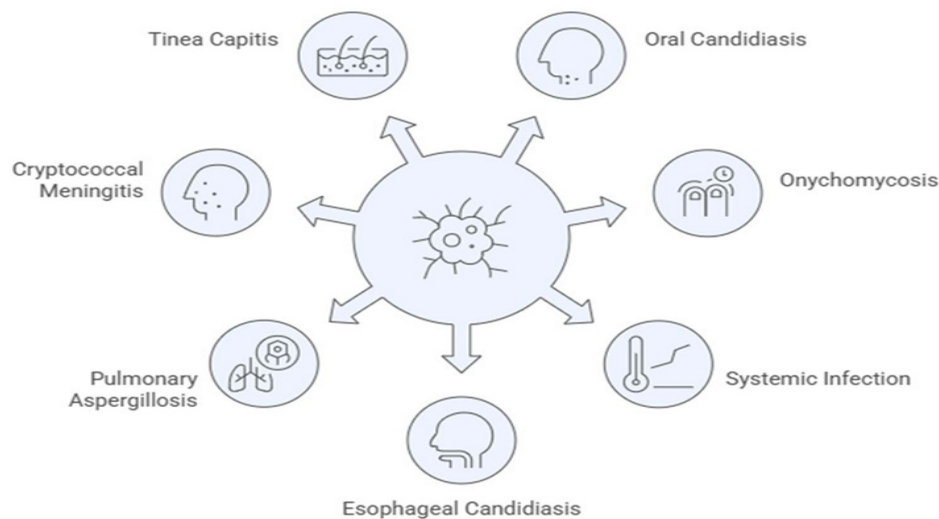
This is one of the most common fungal infections, characterized by creamy white plaques on the oral mucosal surfaces. It is caused primarily by *Candida albicans* and is commonly seen in infants, the elderly, HIV-positive patients, and those on antibiotic or corticosteroid therapy.

7) *Onychomycosis:*

This is a fungal infection of the nails, causing nail thickening, discoloration, brittleness, and separation of the nail from the nail bed. It accounts for nearly 50% of all nail disorders and is one of the primary indications for systemic itraconazole therapy.

III. SYMPTOMS

- 1) Skin Symptoms: Itching, burning, and redness of skin or nails
- 2) Oral Candidiasis: White curd-like plaques on oral mucosa, pain while swallowing
- 3) Onychomycosis: Nail thickening, discoloration, brittleness, and onycholysis
- 4) Systemic Infection: Persistent fever unresponsive to antibiotics
- 5) Esophageal Candidiasis: Difficulty swallowing (dysphagia), chest pain, weight loss
- 6) Pulmonary Aspergillosis: Cough, chest pain, haemoptysis, and breathlessness
- 7) Cryptococcal Meningitis: Headache, neck stiffness, confusion, and altered sensorium
- 8) Tinea Capitis: Hair loss with scaling, broken hair shafts, lymphadenopathy



IV. CAUSES

- 1) Weakened immune system due to HIV/AIDS, cancer, diabetes, or organ transplant
- 2) Prolonged use of broad-spectrum antibiotics that disrupt normal microbial flora
- 3) Long-term corticosteroid or immunosuppressive therapy
- 4) Environmental exposure to fungal spores (soil, bird droppings, decaying matter)
- 5) Poor personal hygiene, excessive sweating, and wearing tight or wet clothing
- 6) Trauma or injury that introduces fungi into the skin or subcutaneous tissue
- 7) Hospitalization and use of invasive medical devices like catheters and ventilators
- 8) Nutritional deficiencies that impair immune function
- 9) Hot and humid climate that promotes fungal growth and proliferation
- 10) Old age, as immunity naturally declines with advancing age

V. PATHOPHYSIOLOGY

A. Candidiasis:

- 1) Candida albicans normally lives harmlessly in the oral cavity, gut, and vaginal mucosa.
- 2) When host defenses are weakened, Candida shifts from yeast form to invasive hyphal form.
- 3) The hyphal phospholipases form in vades mucosal epithelium using secreted enzymes (proteases and
- 4) Inflammatory response generates the characteristic white plaques and redness seen in oral thrush.
- 5) In severe cases, Candida enters the bloodstream (candidemia) and spreads to internal organs.
- 6) Liver, spleen, kidneys, eyes, and heart are commonly involved in disseminated candidiasis.
- 7) Biofilm formation on catheters and medical devices makes the infection very difficult to treat.

B. Dermatophytosis:

- 1) Dermatophyte spores (arthrospores) adhere to the keratinized surface of skin, hair, or nails.
- 2) The organism produces keratinases that breakdown keratin, allowing it to penetrate the tissue.
- 3) Infection spreads outward in a circular pattern, forming the characteristic ring-shaped lesion.
- 4) Host immune response (delayed hypersensitivity) causes inflammation, itching, and scaling.
- 5) In nail infections, the organism invades through the nail plate and destroys the nail bed.
- 6) Chronic, relapsing course is common, especially in toenail infections (onychomycosis).
- 7) Systemic spread is rare in healthy individuals but possible in immunocompromised patients.

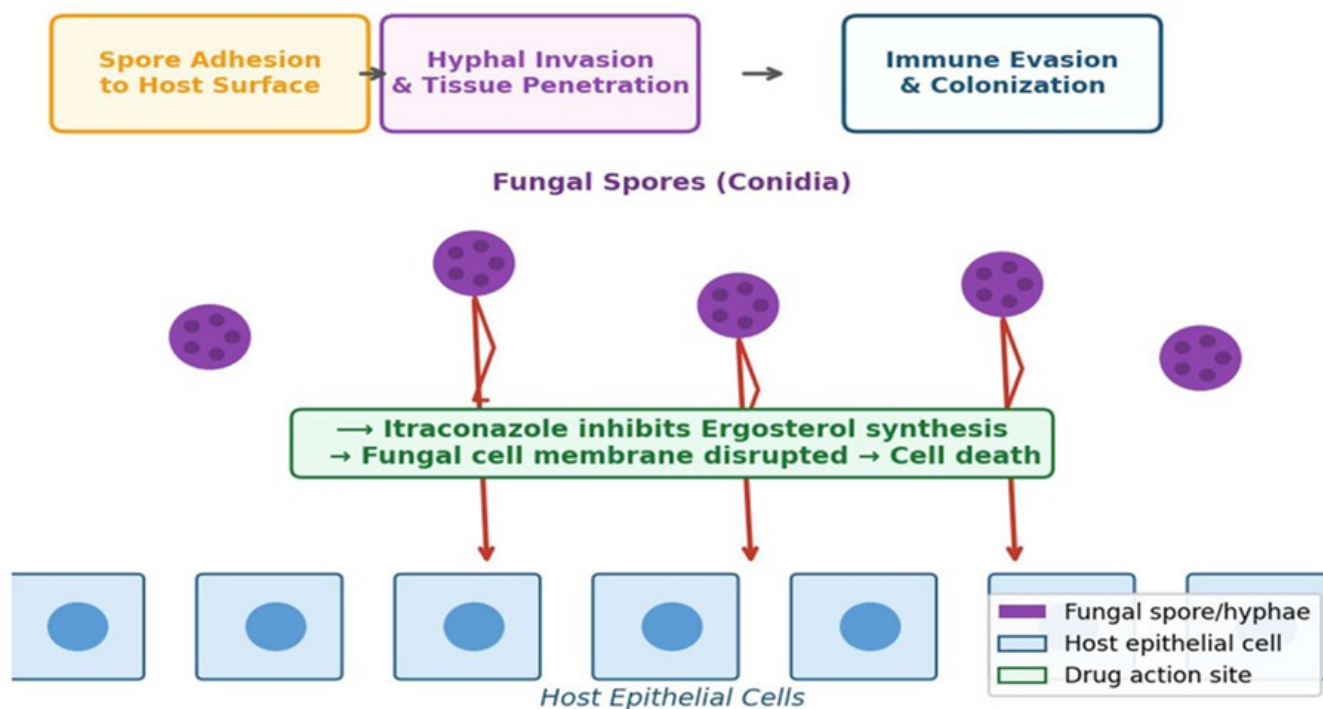


Fig No.2

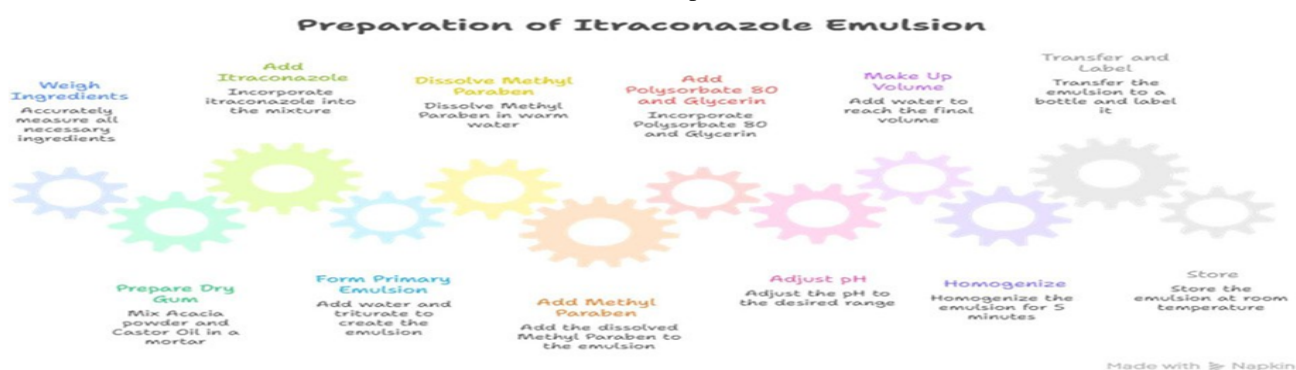
VI. MATERIAL

- 1) Drug: Itraconazole IP
- 2) Excipients: Castor Oil IP, Acacia IP, Polysorbate 80, Glycerin IP, Methyl Paraben IP, Citric Acid IP, Purified Water IP.
- 3) Equipment: Beaker, Glass Rod, Mortar and Pestle, Separating Funnel, Tripod Stand, Water Bath, Test Tubes, Measuring Cylinder, Funnel, Filter Paper.
- 4) Instruments: Weighing Balance, pH Meter, Brookfield Viscometer, Optical Microscope, Homogenizer.

VII. METHOD

Preparation of Itraconazole Emulsion by Dry Gum Method:

- 1) Accurately weigh all ingredients as per the formulation table.
- 2) Take Acacia IP powder in a dry mortar and pestle—this is the dry gum.
- 3) Add Castor Oil to the Acacia powder and triturate well to form a smooth, uniform mixture.
- 4) Add itraconazole to the oil-acacia mixture and continue trituration until the drug is evenly distributed.
- 5) Add one-third of the total water quantity all at once and triturate vigorously until a white, creamy primary emulsion is formed (you will hear a characteristic clicking sound—this confirms primary emulsion formation).
- 6) Dissolve Methyl Paraben IP in a small quantity of warm purified water and add to the primary emulsion.
- 7) Add Polysorbate 80 and Glycerin IP to the emulsion with continuous stirring.
- 8) Adjust pH to 4.5–5.0 using Citric Acid IP solution.
- 9) Make up the volume to 30 mL with Purified Water IP and homogenize for 5 minutes.
- 10) Transfer to a clean amber-colored bottle, label, and store at room temperature.



VIII. DRUG PROFILE

Itraconazole

Official Name: Itraconazole (as per IP, USP, BP)

Chemical Name: (2R,4S)-rel-1-(Butan-2-yl)-4-[4-[4-[(2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)methyl]-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-4,5-dihydro-1H-1,2,4-triazol-5(4H)-one

Molecular Formula: $C_{35}H_{38}Cl_2N_8O_4$ Molecular Weight: 705.64 g/mol Category: Antifungal Agent—Triazole class

Drug Class: BCSC Class II (High Permeability, Low Solubility)

Description:

- Colour: White to almost white powder.
- Odour: Practically odourless.
- Taste: Practically tasteless.
- Melting Point: Approximately 165–169°C.

Solubility:

- Practically insoluble in water ($<1\mu\text{g/mL}$ at physiological pH).
- Slightly soluble in alcohol and dilute hydrochloric acid.
- Freely soluble in dichloromethane and dimethylformamide.
- Solubility increases markedly in acidic pH.

It reacts with lanosterol 14- α demethylase, a cytochrome P450-dependent enzyme in the fungal cell membrane. This enzyme is responsible for converting lanosterol to ergosterol, the main structural sterol of the fungal cell membrane. Inhibition of this enzyme depletes ergosterol and causes accumulation of toxic methylated sterol precursors, leading to disruption of the fungal cell membrane integrity and ultimately fungal cell death.

Pharmacokinetics:

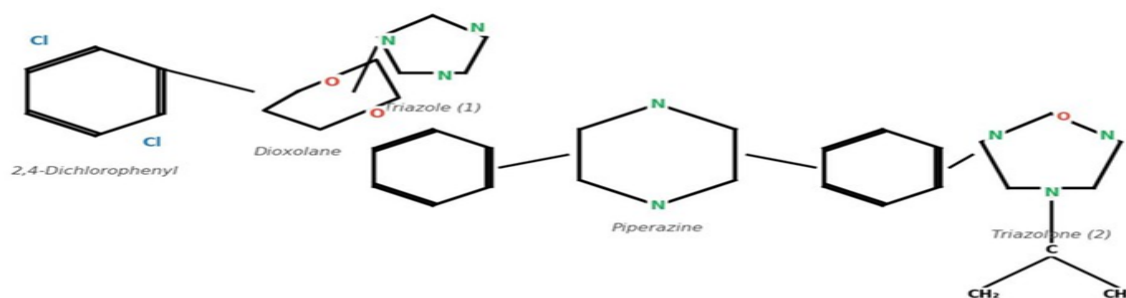
- Absorption: Enhanced when taken with food or in acidic conditions.
- Distribution: Extensively distributed in tissues ($V_d = 796L$); protein binding $>99\%$.
- Metabolism: Extensively metabolized in the liver by CYP3A4 enzyme.
- Elimination: Excreted primarily in feces (54%) and urine (35%) as metabolites.
- Half-life: 16–28 hours after multiple doses.

Indications:

- Oral candidiasis and esophageal candidiasis
- Onychomycosis (nail fungal infections)
- Dermatophytosis (tinea corporis, tinea pedis, tinea cruris)
- Invasive aspergillosis
- Histoplasmosis and blastomycosis
- Prophylaxis of fungal infections in immunocompromised patients

Storage: Store below $25^{\circ}C$, protected from light and moisture.

Itraconazole — Chemical Structure
($C_{35}H_{38}Cl_2N_8O_4$ | MW: 705.64 g/mol)

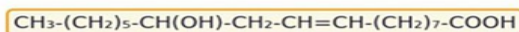
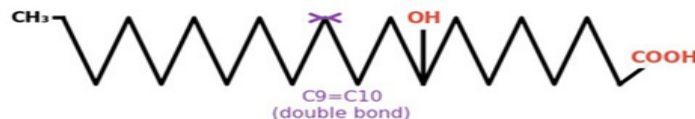
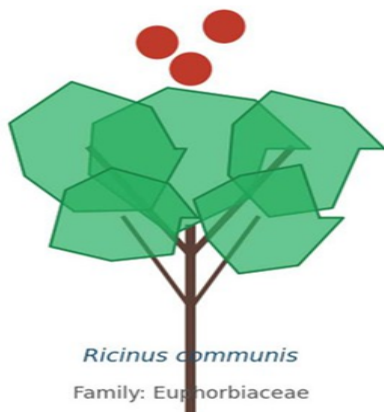


IX. EXCIPIENTS

1) *Castor Oil IP*

Official Name: Castor Oil (IP, BP, USP)

Biological Source: Fixed oil obtained by cold expression of seeds of *Ricinus communis* Linn., Family: Euphorbiaceae.



Chemical Constituents:

- Ricinoleic acid (85–90%)—major fatty acid
- Linoleic acid (4–5%)
- Oleic acid (3%)
- Palmitic acid and Stearic acid (minor amounts)
- Glycerides of fatty acids

Morphological Characteristics:

- Colour: Pale yellow to almost colourless, viscous liquid.
- Odour: Faint, characteristic odour.
- Taste: Bland, slightly nauseating oily taste.
- Consistency: Viscous, oily liquid at room temperature.

Solubility:

- Miscible with dehydrated alcohol, glacial acetic acid, ether, and chloroform.
- Insoluble in water and petroleum ether.

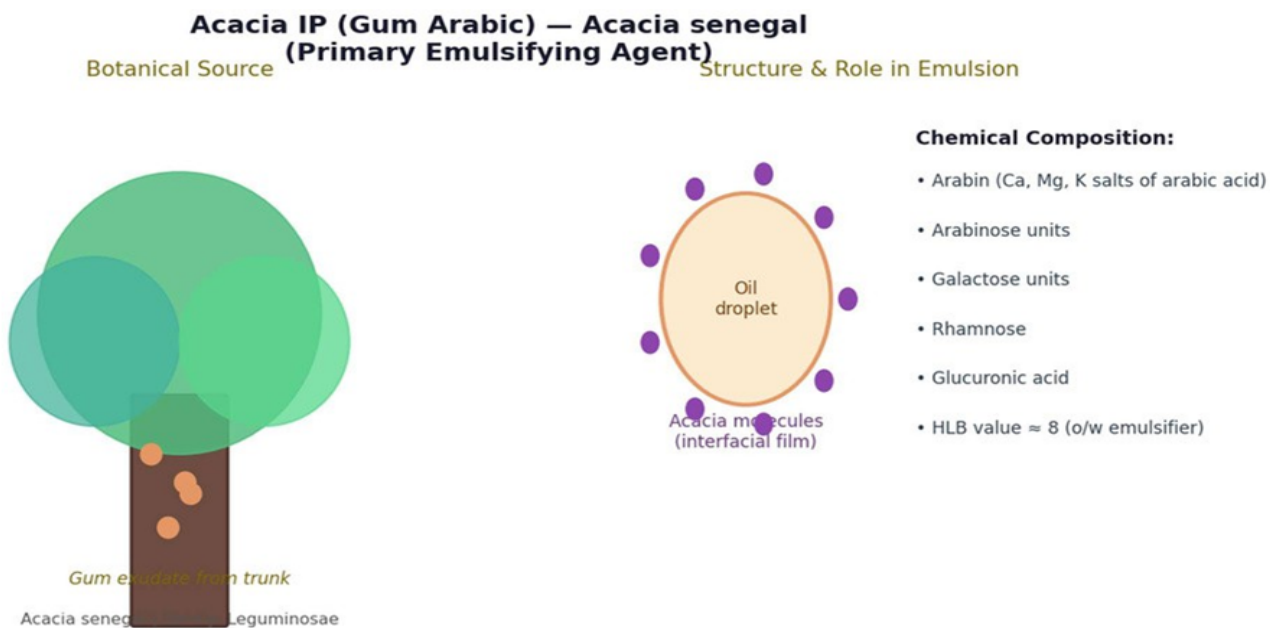
Uses:

- Oil phase in emulsion formulations—excellent solubilizing capacity for poorly soluble drugs.
- Used as a laxative in higher doses.
- Emollient and lubricant in pharmaceutical formulations.
- Vehicle for poorly water-soluble drugs in oral and topical preparations.

2) Acacia IP

Official Name: Acacia (IP, BP, USP)—also known as Gum Arabic

Biological Source: Gummy exudate obtained from the stems and branches of *Acacia senegal* (Linn.) Willdenow or related species, Family: Leguminosae.



Chemical Constituents:

- Arabin—calcium, magnesium, and potassium salts of arabinic acid
- Arabinose, Galactose, Rhamnose, Glucuronic acid
- Oxidases (trace enzymes)
- Moisture content: not more than 15%

Morphological Characteristics:

- Colour: White to yellowish-white tears, flakes, or powder.
- Odour: Odourless.
- Taste: Bland, mucilaginous.
- Texture: Brittle, translucent pieces (tears) or off-white powder.

Solubility:

- Freely soluble in water, forming a viscous, mucilaginous solution.
- Practically insoluble in alcohol and organic solvents.

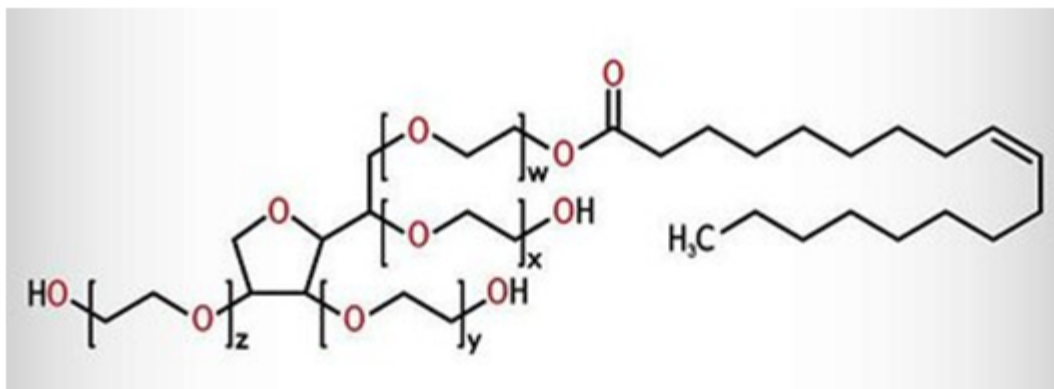
Uses:

- Primary emulsifying agent in oral oil-in-water emulsions—forms a strong interfacial film.
- Binding agent in tablets.
- Suspending and thickening agent in oral liquid preparations.
- Demulcent to soothe irritated mucous membranes.

3) *Polysorbate 80 (Tween 80)*

Official Name P: polysorbate 80 (IP, USP, BP)

Chemical Name: polyoxyethylene (20) sorbitan monooleate



Molecular Formula: $C_{64}H_{124}O_{26}$ Molecular Weight: 310 g/mol

HLB Value: 15—strongly hydrophilic character, ideal for o/w emulsions

Category: Non-ionic surfactant, Co-emulsifier, Solubilizer, Stabilizer

Description:

- Colour: Amber-yellow to orange oily liquid.
- Odour: Faint, characteristic.
- Consistency: Viscous liquid.

Solubility:

- Freely soluble in water, ethanol, and methanol.
- Miscible with oils and aromatic hydrocarbons.

Uses:

- Co-emulsifier in oral and topical emulsion formulations—boosts HLB of emulsifier system.
- Solubilizer for poorly water-soluble drugs.
- Wetting agent and dispersing agent.
- Stabilizes emulsion against droplet coalescence and phase separation.

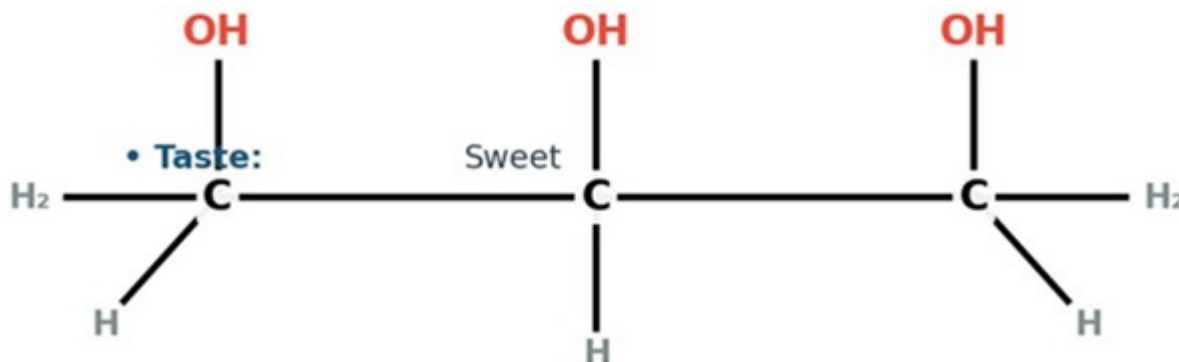
4) *Glycerin IP*

Official Name G: glycerin (IP, USP)/Glycerol (Ph.Eur.)

Chemical Name Per: propane-1,2,3-triol Molecular Formula $C_3H_8O_3$

Molecular Weight: 2.09 g/mol

Category: Humectant, Viscosity builder, Sweetening agent, Pharmaceutical excipient



Description:

- Colour: Clear, colourless, viscous liquid.
- Odour: Odourless.
- Taste: Sweet, warm.
- Nature: Hygroscopic—absorbs moisture from the atmosphere.

Solubility:

- Freely soluble in water and alcohol.
- Miscible with chloroform and propylene glycol.
- Practically insoluble in oils and fats.

Uses:

- Humectant—prevents drying out of the emulsion during storage.
- Viscosity builder—increases the viscosity of the aqueous phase, slowing droplet movement and preventing phase separation.
- Sweetening agent in oral liquid preparations.
- Co-solvent for drugs in oral formulations.
- Emollient and plasticizer in pharmaceutical formulations.

5) *Methyl Paraben IP*

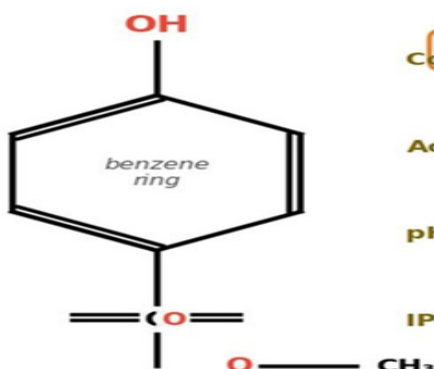
Official Name M: ethylparaben (IP, USP, BP)—also known as Methyl 4-hydroxybenzoate

Chemical Name Me: ethyl 4-hydroxybenzoate

Molecular Formula $C_8H_8O_3$

Molecular Weight: 52.15g/mol

Category: Antimicrobial preservative, Pharmaceutical excipient, Food preservative (E218)



Category:	Antimicrobial preservative
Conc. used:	$\text{HO}-\text{C}_6\text{H}_4-\text{COOCH}_3$ 0.1% w/w in formulation
Activity:	Bacteriostatic + Fungistatic
pH stability:	Effective at pH 3-8
IP standard:	IP grade — meets all specifications

Description:

- Colour: White, crystalline powder or colourless crystals.
- Odour: Practically odourless or very faint characteristic odour.
- Taste: Slightly burning.

Solubility:

- Soluble in ethanol, ether, acetone, and propylene glycol.
- Slightly soluble in water (about 0.25% at 25°C).
- Freely soluble in alkaline solutions due to salt formation.

Uses:

- Widely used as antimicrobial preservative in oral liquid and topical pharmaceutical preparations.
- Effective against bacteria, yeasts, and molds.
- Used at 0.1-0.18% in oral formulations as per IP guidelines.
- Often combined with propylparaben for broader spectrum preservation.

6) Citric Acid IP

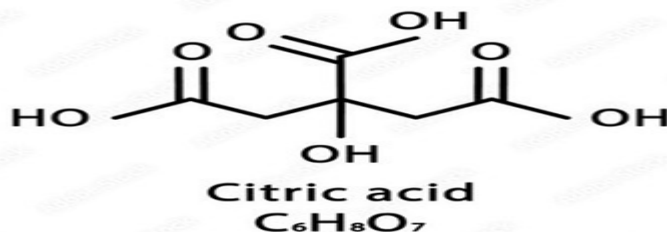
Official Name: Citric Acid Monohydrate (IP, USP, BP)

Chemical Name: 2-hydroxy-1,2,3-propane-tricarboxylic acid

Molecular Formula: Anhydrous: $\text{C}_6\text{H}_8\text{O}_7$ | Monohydrate: $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$

Molecular Weight: Anhydrous: 192.12g/mol | Monohydrate: 210.14g/mol

Category: Acidulant, pH adjuster, Antioxidant synergist, Chelating agent, Buffering agent, Food additive (E330)



Description:

- Colour: Colourless, odourless crystals or white crystalline powder.
- Odour: Odourless.
- Taste: Strong, pleasant acid taste.

Solubility:

- Freelysolubleinwaterandethanol(95%).
- Practicallyinsolubleinetherandchloroform.

Uses:

- pHadjuster—maintainsoptimalpH(4.5–5.0)fordrugstabilityandmucosalcompatibility.
- Antioxidantsynergist—preventsoxidativedegradationoftheemulsioncomponents.
- Chelatingagent—bindsmetalionsthatcouldcatalyzeoxidationreactions.
- Bufferingagentinpharmaceuticalformulations.

X. FORMULATION TABLE

(BatchSize:30mL|AllingredientsareIPgrade)

Sr.

No.

Ingredient Role

- 1) ItraconazoleIP
- 2) CastorOilIP
- 3) AcaciaIP
- 4) Polysorbate80
- 5) GlycerinIP
- 6) MethylParabenIP
- 7) CitricAcidIP
- 8) PurifiedWaterIP
- 9) ActiveAntifungalDrug

OilPhase+Drug Solubilizer

Primary Emulsifying Agent Co-emulsifier+Stabilizer

ViscosityBuilder+ Humectant

Preservative

pHAdjuster(pH4.5–5.0) Vehicle(AqueousPhase)

XI. EVALUATION PARAMETER

1) Organoleptic/PhysicalProperties

This test evaluates the prepared emulsion for its appearance, colour, odour, taste, and consistency. A well-prepared emulsion should be uniform in colour, have a pleasant or acceptable odour, smooth texture, and should show no signs of oiling out, creaming, or phase separation. These properties directly reflect the product's stability and patient acceptability.

2) pH Determination

The pH of the emulsion is measured using a calibrated digital pH meter at room temperature. For oral emulsions, a pH range of 4.5 to 5.5 is considered ideal. This pH range ensures mucosal compatibility, minimizes irritation to the oral and gastric mucosa, and maintains optimal drug stability, since itraconazole degrades in alkaline conditions.

3) Viscosity

Viscosity of the emulsion is measured using a Brookfield Viscometer at a specific spindle speed and temperature (25°C). Appropriate viscosity ensures that the emulsion pours easily for dose administration while remaining stable against phase separation. High viscosity reduces droplet mobility and helps maintain emulsion stability over time.

4) Homogeneity

Homogeneity is assessed by visual examination and microscopic observation of the emulsion. A homogeneous emulsion should be free from lumps, undissolved particles, or visible oil droplets on the surface. It can also be examined by spreading a thin film on a glass slide under an optical microscope to confirm uniform droplet distribution.

5) *CercereaamminngginIndedxeixsd,TEST*

The creaming index is determined by measuring the volume of emulsion in a graduated measuring cylinder and allowing it to stand undisturbed at room temperature for 24 hours. The height of the separated cream or oil layer, if any, is noted and calculated as a percentage of total emulsion height. A lower creaming index indicates better emulsion stability.

6) Droplet Size and Size Distribution

Average droplet size and polydispersity index (PDI) of the emulsion are determined using a particle size analyzer or optical microscope. Smaller droplet size (<10 μm for macroemulsions) ensures better stability, greater surface area for absorption, and improved bioavailability. A narrow size distribution (low PDI) reflects formulation uniformity.

7) Zeta Potential

Zeta potential indicates the electrostatic stability of the emulsion droplets. It is measured using a Zetasizer. A zeta potential value above ±30 mV suggests adequate electrostatic repulsion between droplets, which prevents coalescence and ensures long-term physical stability of the emulsion.

8) Drug Content Uniformity

Drug content is determined by UV spectrophotometry at the λ_{max} of itraconazole (approximately 258 nm). A known volume of emulsion is diluted with methanol, filtered, and the absorbance is measured. The drug content should be within 90–110% of the labeled amount as per IP specification to ensure accurate dosing and therapeutic consistency.

9) Stability Studies

Accelerated stability studies are carried out as per ICH Q1A(R2) guidelines. Samples are stored at 40°C ± 2°C / 75% RH ± 5% for 3 months. Physical appearance, pH, viscosity, creaming index, and drug content are evaluated at 0, 1, 2, and 3-month intervals. Stable formulations show no significant changes in these parameters throughout the study period.

10) Centrifuge Test (Physical Stability)

Centrifugation at 3500 rpm for 30 minutes is used as an accelerated test for physical stability. The emulsion is examined for any phase separation after centrifugation. Absence of phase separation indicates a stable emulsion system that is likely to remain stable during storage and handling.

XII. CHEMICAL TESTS (DRUG IDENTIFICATION—ITRACONAZOLE)

1) Colour Reaction with Sulfuric Acid

Procedure: Dissolve a small quantity of itraconazole in 2 mL of concentrated sulfuric acid. Observation:

A characteristic reddish-brown to brownish coloration is produced, which indicates the presence of itraconazole.

2) Chloride Identification Test

Procedure: Dissolve itraconazole in dilute nitric acid and add a few drops of silver nitrate solution.

Observation: Formation of a white curdy precipitate of silver chloride, which is soluble in dilute ammonia, confirms the presence of chloride atoms in the molecule.

3) Triazole Ring Test

Procedure: Dissolve itraconazole in methanol and add a few drops of copper sulfate solution and sodium hydroxide.

Observation: Formation of a characteristic complex color confirms the presence of the triazole ring structure in the molecule.

4) Emulsion Drug Release (In-vitro Dissolution)

Procedure: Place 5 mL of emulsion in 500 mL simulated gastric fluid (pH 1.2) or simulated intestinal fluid (pH 6.8) in a dissolution apparatus. Withdraw 5 mL samples at 15, 30, 45, 60, and 90 minutes. Filter and measure absorbance by UV spectrophotometry at 258 nm.

Observation: Drug release profile is plotted. The emulsion should show significantly faster and more completed drug release compared to conventional itraconazole capsules.

XIII. DRUG-EXCIPIENT COMPATIBILITY STUDY

Sr.No.	Test	Method Used	Observation
1	Itraconazole + Castor Oil	Visual & IR Spectroscopy	No physical incompatibility observed — clear solution formed
2	Itraconazole + Acacia IP	Visual examination after 48 hours	No discoloration or precipitation — compatible
3	Itraconazole Polysorbate 80	+ Visual & solubility test	Enhanced solubilization observed — no incompatibility
4	Itraconazole + Glycerin IP	Visual & DSC	No interaction — stable mixture
5	Itraconazole + Methyl Paraben	Visual after 1 week at 40°C	No colour change or degradation — compatible
6	Itraconazole + Citric Acid	pH monitoring over 7 days	Stable at pH 4.5–5.0 — no degradation observed

XIV. CONCLUSION

Itraconazole-based oil-in-water emulsion represents a highly promising and pharmaceutically innovative approach for the oral delivery of this poorly water-soluble antifungal drug. The formulation was successfully prepared using minimal Indian Pharmacopoeia grade excipients—Castor Oil IP as the oil phase, Acacia IP and Polysorbate 80 as the emulsifying system, and Glycerin IP as a viscosity-enhancing stabilizer—in a 30 mL batch size.

The dry gum method of emulsion preparation produced a stable, uniform, and creamy white emulsion with no phase separation. The optimized formulation demonstrated acceptable physicochemical properties including appropriate pH (4.5–5.0), adequate viscosity, uniform droplet size distribution, satisfactory drug content, and good physical stability on accelerated testing.

The emulsion dosage form effectively overcomes the major limitations of conventional itraconazole capsules namely poor and erratic oral bioavailability—by pre-dissolving the drug in the oil phase and enhancing absorption through the lymphatic pathway. This approach minimizes first-pass hepatic metabolism and produces more reliable and consistent therapeutic drug levels in the bloodstream.

Furthermore, the liquid nature of the formulation makes it particularly suitable and patient friendly for pediatric patients, elderly individuals, and those with swallowing difficulties, who represent a significant proportion of patients requiring antifungal therapy. The formulation offers the additional advantage of allowing precise, weight-based dosing in children.

In conclusion, the itraconazole antifungal emulsion formulated using IP grade excipients stands as a safe, effective, stable, and patient-friendly oral dosage form that offers significant therapeutic advantages over conventional solid formulations, and holds great potential for further development and clinical application in the treatment of fungal infections.

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