INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

Formulation And Evaluation of Miconazole Nitrate Loaded Nanoparticle Gel

Jagadish G., Prajwal R.*, Manasa P., Manoj M., Anju K. P.

Department of Pharmaceutics, Spurthy college of pharmacy.

ARTICLE INFO

Published: 15 Nov 2025
Keywords:
Nanoparticle gel, ionic gelation method, Miconazole Nitrate, antifungal activity
DOI:
10.5281/zenodo.17615314

ABSTRACT

The present research work focuses on the formulation and evaluation of a Miconazole Nitrate-loaded nanoparticle gel designed to enhance skin penetration and improve topical bioavailability for effective antifungal therapy. Miconazole Nitrate is a broad-spectrum imidazole derivative widely used in the treatment of cutaneous mycoses, dermatophytosis, and other fungal infections. However, its low aqueous solubility and limited skin permeability restrict its therapeutic potential when delivered through conventional topical dosage forms such as creams and ointments. To overcome these limitations, a nanoparticle-based delivery system was developed to provide controlled release, increased surface area, and better drug penetration through the skin. In this study, Miconazole Nitrate nanoparticles were prepared by the ionic gelation method, employing chitosan as a biocompatible polymer and sodium tripolyphosphate (STPP) as a cross-linking agent. The optimized nanoparticles were further incorporated into a Carbopol 934 gel base to obtain a stable, user-friendly topical formulation. The prepared nanoparticle gels were evaluated for particle size, zeta potential, pH, viscosity, spreadability, homogeneity, drug content, and entrapment efficiency. The optimized formulation (F2) exhibited a mean particle size of 235 nm, zeta potential of –27.0 mV, and entrapment efficiency of 98.81%, confirming good stability and uniform dispersion. The pH (4.98) and viscosity (10041 mPa·s) were within the acceptable range for topical application, and drug content was found to be 94.98%, indicating excellent drug loading. Scanning Electron Microscopy (SEM) revealed spherical nanoparticles with smooth surfaces. These findings demonstrated improved homogeneity, stability, and skin compatibility compared with conventional Miconazole formulations. Overall, the developed Miconazole Nitrate-loaded nanoparticle gel effectively enhanced drug encapsulation and potential skin permeation while maintaining desirable physical and rheological properties. This novel formulation offers a promising approach for the topical treatment of fungal infections, providing sustained drug release, better patient compliance, and improved therapeutic efficacy.

***Corresponding Author:** Prajwal R.
Address: *Department of Pharmaceutics, Spurthy college of pharmacy.*
Email ✉: prajwalr5605@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Future studies involving in-vitro release kinetics, antifungal activity, and skin permeation studies are suggested to establish the clinical potential of the developed nanoparticle gel.

INTRODUCTION

1.1 Topical drug delivery: -

Topical drug delivery system is traditional drug delivery system having a history of more than thousand years.in ancient Days ointment and salves are made from plant, animal and mineral extract. These preparations are delivered through topical route for treatment of skin diseases. This method was employed by Chinese, Egyptians and Babylonians.[1] The skin acts as a barrier for the entry and exit of many chemicals, prevents moisture loss and control body temperature to maintain homeostasis with in the body. Topical preparations are useful in preventing gastric degradation of drug and avoids first pass metabolism.so, there is increase in bioavailability of the drug and these tropical preparations give its action directly at the site of action.[2]

Various Topical Formulations Available In Market Are Listed Below: -

- Semi -Solid preparations: -

Eg: - Gels, Paste, Creams, Ointments.

- Liquid Preparations: -

Eg: - Lotions, Solutions, Liniments.

- Solid Preparations: -

Eg: - Powders.

- Other Preparations: -

Eg: - Transdermal patches, Foams, Sprays, etc.[3]

Benefits Of Topical Drug Delivery System: -

→ Avoidance of First-Pass Metabolism.

→ Targeted, Localized Therapy.

→ Improved Patient Compliance.

→ Reduced Systemic Side Effects.

→ Patient-Friendly Formulations.

→ Lower Dose and Enhanced Efficacy.

→ Non-Invasive and Easily Reversible.

→ Controlled or Sustained Release Possibilities.[4]

1.2 Anatomy and physiology of skin: -

The largest organ of human body is skin it covers about 15% of total adult body weight it performs many important functions like protection against external physical, chemical and biological agents, it prevents excessive water loss from the body. The skin is composed of three main layers: -1) Epidermis, 2) Dermis and 3) Subcutaneous fascia .[5] Epidermis is the outermost layer of the skin having different layers such as stratum spinosum, stratum granulosum, stratum lucidum, stratum basale. Cells of epidermis includes keratinocytes, melanocytes, langerhans and marker cells. Dermis is a second layer of skin which is connected to epidermis by the basement membrane. The dermis is made up of two layers of connective tissue, the reticular and papillary, which blend together without obvious separation. The higher dermal layer, known as the papillary layer, is thinner and made up of loose connective tissue that comes into touch with the epidermis. The deeper, thicker, and less cellular layer is called the reticular layer. Collagen fiber bundles make up the dense connective tissue that makes up this layer. Hypodermis also known as Subcutaneous fascia, it is located beneath the dermis so it is called as hypodermis. It is the deepest layer of the skin, it

consists of sensory neurons, blood vessels, hair follicle and adipose lobules.[6]

The skin structure and physiology play a crucial role in the delivery and permeation of drug via this route. The presence of hair follicles and pores plays a critical role in drug permeation.[7] Stratum Corneum is layer of skin composing of 40% lipids, 40% proteins and only 20% water. So, this composition helps in permeation of liphophillic drug. This liphophillic character of drug suitable for topical delivery of drugs. However hydrophilic drugs are difficult to pass through stratum corneum due to its less water content. Here the hair follicles and pores play role in the absorption of drugs.[8]

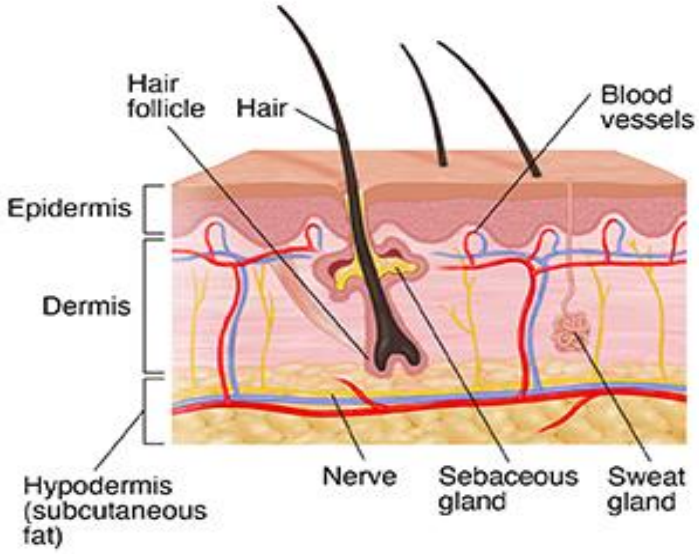

Fig 1.1: - Structure of Skin

1.3 Diseases: -

1). Superficial infections: -

It is an infection caused by pathogenic fungi which affects human hair, nails, epidermis, and mucosa. Dermatophytosis, pityriasis vercicolor, superficial candidiasis are the common types of superficial fungal infection.[9]

- **Dermatophytosis: -**

It is a fungal infection caused by epidermophyton, microsporum and trichophyton. Dermatophytes usually attack and parasitize only on the keratinized layers of skin, nail, and hair. Dermatophyte infections are also known as Tinea infections are commonly seen all over the world. On the global scale Tinea, Rubrum is currently identified as the main cause of fungal infections that cause cutaneous and oncomycosis.[10]

- **Superficial candidiasis: -**

Skin infections and infections of the nails and adjacent tissues (onychomycosis and paronychia) are examples of superficial candidiasis. Candida skin infections are frequently found in intertriginous areas, including under the breasts, fingertips, and the crevices between skin folds in the groin and under the arms.[11]

It includes infection of mucocutaneous or cutaneous tissues. The causative agent of superficial candididis is Candidida albicans, Other candidia species causes superficial infection

includes C. tropicalis, C. glabrata, C. parapsilosis. Superficial candidiasis can be acute, chronic or recurrent. It includes skin, oropharyngeal, gastro intestinal, vaginal and conjuctival tissue infection.[12]

For candidiasis wide range if nanoparticles are used effectively those are chitosan nanoparticles, silver nanoparticles, zinc oxide nanoparticles, lipid-based nanoparticles.[13]

- **Pityriasis vercicolor: -**

Pityriasis vesicolor is a superficial fungal infection of the skin which is caused by Malassezia which is a liphophillic dimorphic fungus. This fungus is a normal part of skin flora but can cause disease when it converts to its pathogenic hyphal form. This conversion will happen by certain environmental, genetic and immunological factors and contributes to cause the disease. There is a significant increase in the disease between children's and adolescence because of the hormonal changes that increase in the sebum production and allow for more lipid rich environment in which the fungus can grow.[14]

1.4 Novel approaches in treatment of fungal diseases: -

Novel approaches include nanoparticle gel, liposomes, neosomes, transporosomes etc., of this nanoparticle technology is a rapidly growing technology in the field of pharmaceutics. Nanoparticle is incorporated into the gel which is termed as 'Nanogel'. These Nanoparticle are prepared by "emulsion diffusion method".

For the preparation of Nanoparticle Nanogel the API used is Miconazole nitrate.[15]

1.4.1 Gel: -

As per USP Gels are defined as a semi solid system containing either suspensions made up of small organic or inorganic molecules interpenetrated by a liquid. These are the preparation which are intended for application on the skin. Gels are generally considered to be more rigid because gels contain more covalent cross links, a higher density of physical bonds. [16] A gel consists of natural or synthetic polymers forming a three-dimensional matrix throughout a hydrophilic liquid or a dispersion medium. A gel is made up of two layers cross-linked, three-dimensional substance that contains a significant volume of liquid to create a stiff network which immobilizes the liquid continuous phase.

Ideal properties of topical gel:

- Gel should be clear and homogenous.
- Should be inert in nature.
- It should be stable, nonirritant.
- It should be non-sticky.
- It should have anti- microbial activity.

Advantages of Gel: -

- It can be used as controlled release formulation.
- They can be used to administer both polar and non-polar drugs.
- Easy to formulate as compared to other semi solid dosage form.
- They are biodegradable and biocompatible.
- They are washable and nontoxic in nature.
- Retention time is higher than other topical dosage forms.

- They provide excellent spread ability and cooling effect.

DISADVANTAGES: -

- Some drug may degrade in gel formulation due to presence of polymer.
- Gelling agent may precipitate and result in salting out.
- Flocculation in some gel may produce an unstable gel.
- Solvent evaporation from the formulation may result in drying of the gel.
- The additives may induce irritation.
- The water content may increase the chances of microbial or fungal attack in gel.[16]

1.5 Nanoparticle gel: -

Nanoparticle gels are semisolid systems where nanoparticles are embedded within a gel matrix, combining enhanced solubility, stability, and controlled release of therapeutic agents with easy topical application and prolonged residence time.[17] These systems bolster penetration, bioavailability, and patient compliance while enabling sustained and targeted delivery. They find applications across pharmaceuticals—antifungal, antibacterial, anti-inflammatory therapies—and advanced biomedicine, including wound healing, tissue regeneration, and localized cancer treatment.[18]

1.6 Method of preparation of nanoparticles: -

Nanoparticles can be formulated by various methods like ion gelation method, solvent evaporation method, micro emulsion technique, Nano precipitation method, solvent diffusion method, emulsification method,

A. Ion gelation method: -

Nanoparticles were produced using the ionotropic gelation method, a simple and widely accepted technique for fabricating polymeric carriers. In this approach, chitosan was first dissolved in dilute acetic acid with constant stirring to yield a transparent cationic polymer solution. A stabilizer such as Tween 80 or poloxamer was incorporated to enhance homogeneity and reduce aggregation. Separately, sodium tripolyphosphate (TPP) was dissolved in distilled water to act as a polyanionic cross-linker. The TPP solution was then added dropwise into the chitosan dispersion under moderate magnetic stirring. Electrostatic interactions between the positively charged amino groups of chitosan and the negatively charged phosphate groups of TPP triggered spontaneous nanoparticle formation. The suspension was stirred further for 30–60 minutes to ensure complete cross-linking and stabilization. The resulting colloidal system was centrifuged to separate nanoparticles from unbound components, followed by washing and re-dispersion in distilled water. The prepared nanoparticles were stored under refrigerated conditions until use. This method is advantageous because it avoids organic solvents, requires mild processing conditions, and yields biocompatible Nano systems suitable for a wide range of therapeutic applications, particularly for drugs intended for mucosal and topical delivery.[19]

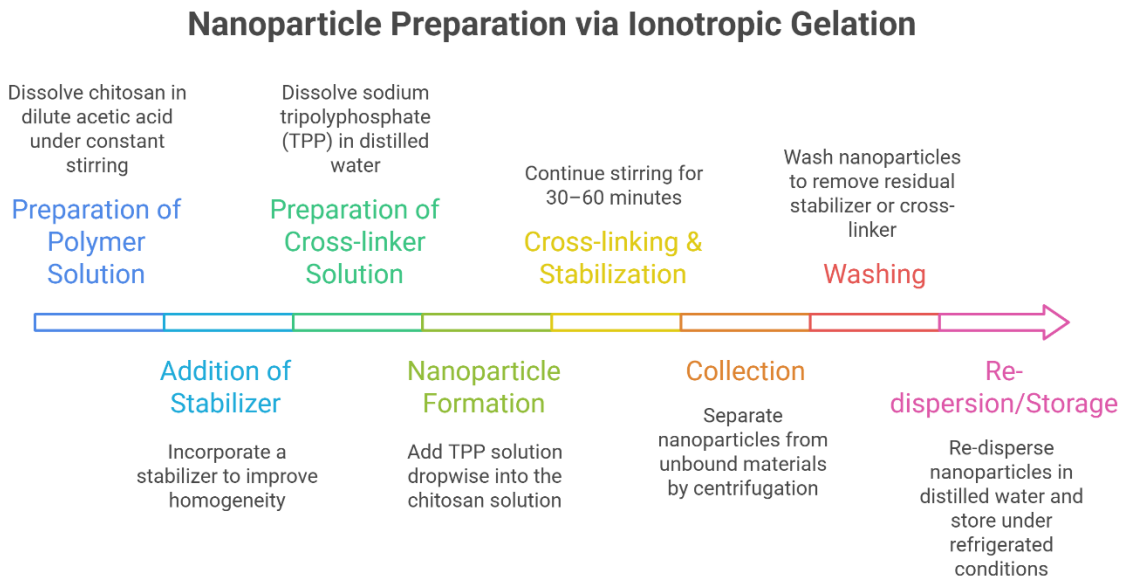

Fig 1.2: - Ion gelation method

B. Solvent evaporation method: -

In the emulsification–solvent evaporation technique, a polymer and the active ingredient are first dissolved in a volatile organic solvent to form the oil phase. This solution is emulsified into an aqueous phase containing a surfactant (e.g., PVA or Tween) using high-shear homogenization or probe sonication to produce an oil-in-water emulsion. Subsequent removal of the organic solvent by stirring, reduced pressure, or evaporation causes polymer precipitation and hardening into nanoparticles. The nanoparticles are collected by centrifugation or ultrafiltration, washed to remove residual surfactant and free drug, and re-dispersed in an appropriate medium. This method is versatile for hydrophobic drugs, allows control of particle size via emulsification energy and stabilizer concentration, and is widely used for PLGA and other polymeric nanoparticle systems.[20]

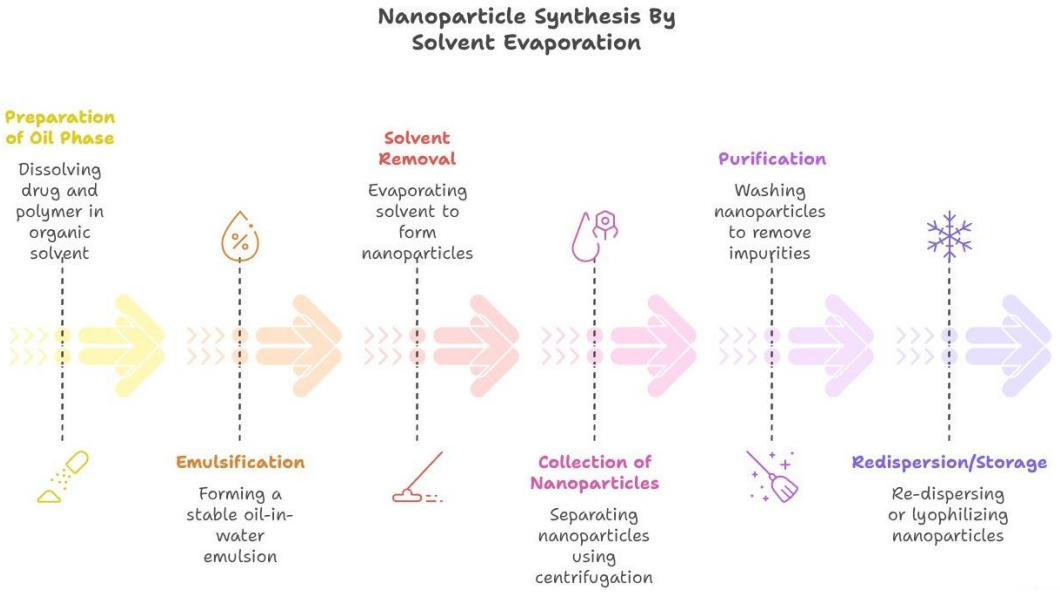

Fig 1.3: -Solvent evaporation method

C. Solvent diffusion method: -

The solvent diffusion technique is a straightforward approach for producing polymeric nanoparticles under mild conditions. In this method, both the drug and a suitable polymer are dissolved in a partially water-miscible organic solvent such as acetone or ethanol. This organic phase is then introduced into an aqueous phase containing a stabilizer under gentle stirring. The difference in solvent polarity leads to rapid diffusion of the organic solvent into the water, which reduces the solubility of the polymer and causes it to precipitate as nanoparticles. The formed colloidal suspension is further stirred to allow complete diffusion of the solvent, which can subsequently be removed by evaporation. The nanoparticles are collected by centrifugation or filtration, washed, and re-dispersed in water for storage. This method is advantageous as it avoids high energy inputs, yields uniform particle size, and is particularly effective for hydrophobic drugs.[21]

Fig 1.4: - Solvent diffusion method

D. Microemulsion method: -

The microemulsion method is a reliable approach for fabricating nanoparticles using thermodynamically stable dispersions. In this technique, an oil phase containing the drug and polymer or lipid is mixed with a surfactant and co-surfactant system to form a transparent microemulsion. The aqueous phase is then added under constant stirring, which triggers rapid precipitation of the dispersed phase as nanoparticles due to changes in solubility and interfacial tension. The nanoparticles formed are stabilized by the surfactant layer, preventing aggregation. Residual solvents are removed by gentle heating or evaporation, and the particles are collected by centrifugation or filtration. This method is advantageous because it operates under mild conditions, offers reproducible particle sizes in the nanometer range, and allows the incorporation of both hydrophilic and lipophilic drugs for controlled release applications.[22]

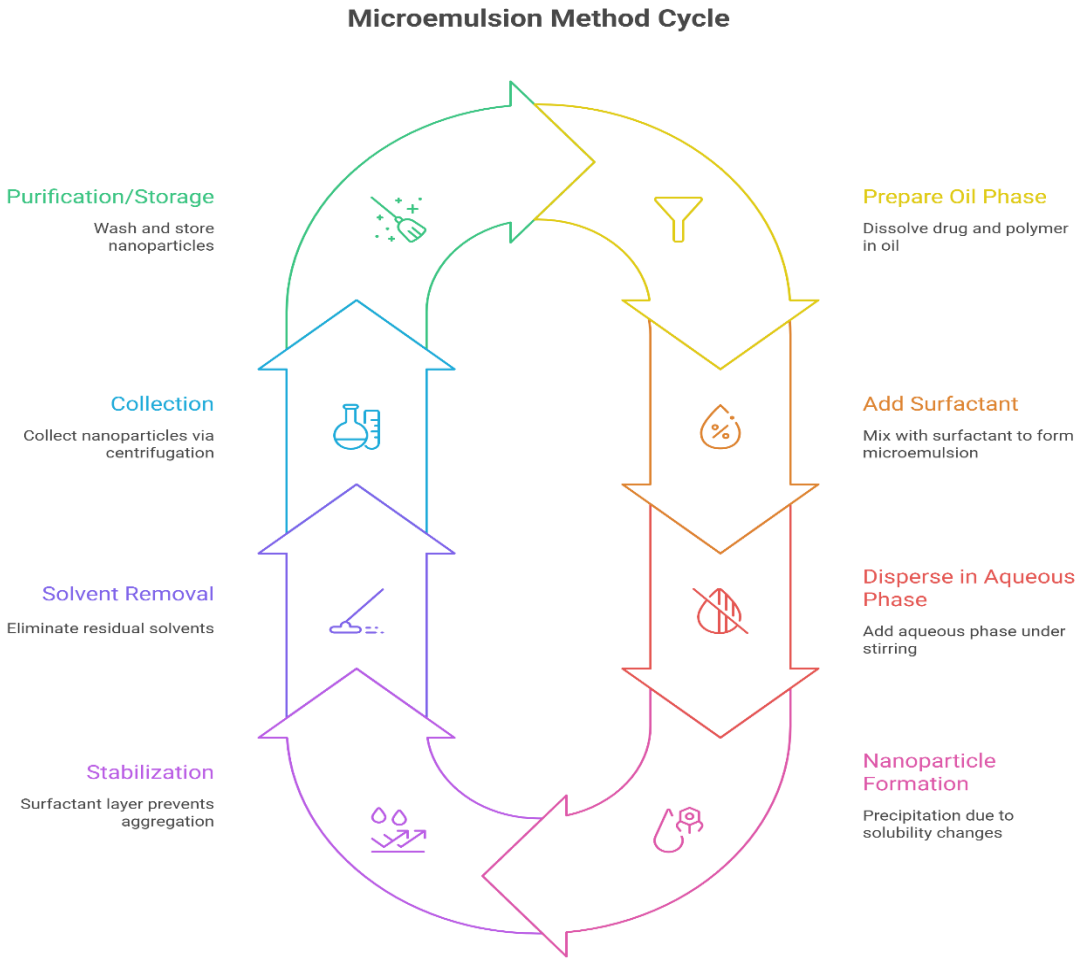

Fig 1.5: - Microemulsion method

E. Nanoprecipitation method: -

The nanoprecipitation technique, also called solvent displacement, is one of the most widely used methods for preparing polymeric nanoparticles. In this approach, the polymer and drug are dissolved in a water-miscible organic solvent such as acetone or ethanol. This solution is then introduced dropwise into an aqueous phase containing a stabilizer, under gentle stirring. The rapid diffusion of the organic solvent into water

lowers polymer solubility, leading to spontaneous formation of nanoparticles. Surfactants or stabilizers adsorb onto the particle surface, preventing aggregation and ensuring a narrow size distribution. Once the solvent diffuses completely, it can be removed by evaporation under reduced pressure or mild heating. The resulting nanoparticles are collected by centrifugation and re-dispersed in water. This method is favored because it is simple, energy-efficient, and produces small, uniform particles suitable for encapsulating hydrophobic drugs.[23]

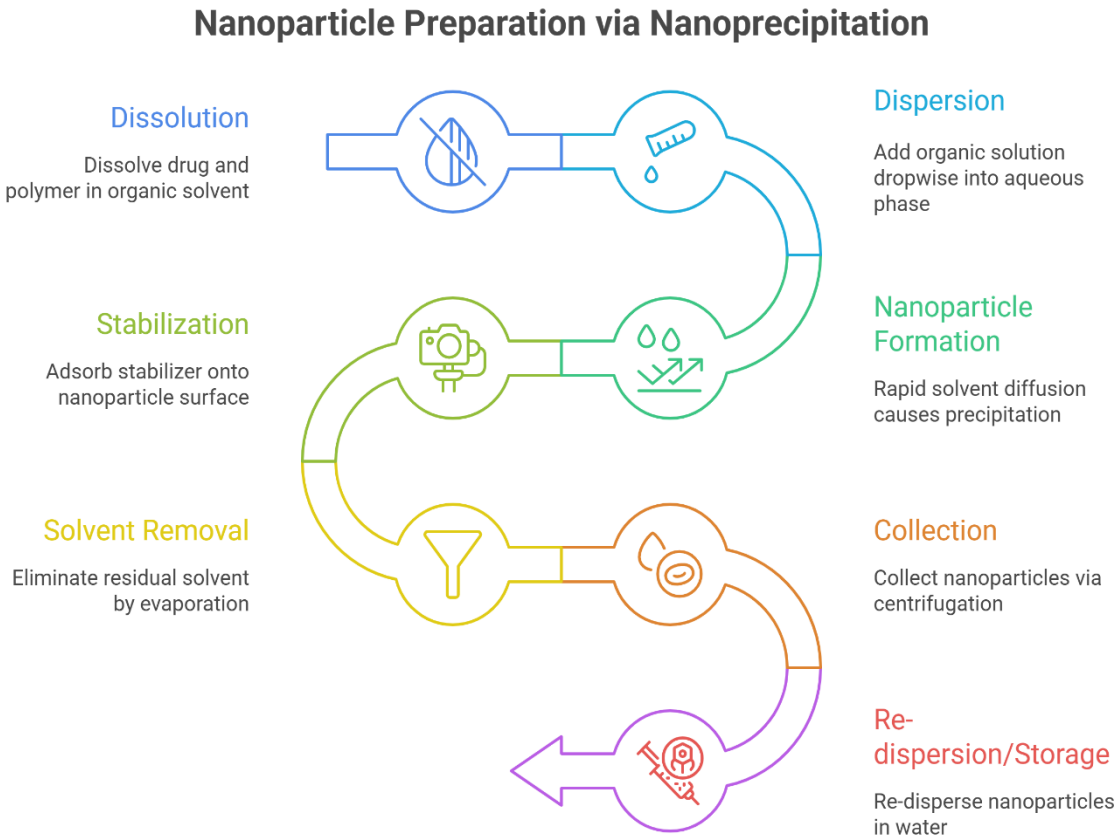

Fig 1.6: - Nanoprecipitation method

F. Emulsification method: -

The emulsification method is a versatile technique commonly employed for the preparation of polymeric and lipid-based nanoparticles. In this approach, the drug and polymer or lipid are first dissolved in an organic solvent, which is then emulsified into an aqueous phase containing a suitable surfactant under high-speed homogenization or ultrasonication. This process creates an oil-in-water emulsion with fine droplets, within which the drug becomes entrapped. Subsequently, the organic solvent is removed either by evaporation or diffusion, resulting in the hardening of the droplets into stable nanoparticles. The final product is purified through centrifugation and re-dispersed in distilled water. This method offers the advantage of good drug entrapment efficiency, controlled particle size, and suitability for both hydrophilic and lipophilic drugs, making it highly applicable in pharmaceutical formulations.[24]

Fig 1.7: - Emulsification method

1.7 Drug profile: -

Miconazole Nitrate: -

Miconazole nitrate is an azole-based antifungal agent known for its broad-spectrum activity. It is commonly prescribed to manage fungal infections of the skin, mouth, and vagina, particularly in cases of candidiasis. While intravenous formulations are no longer available, the drug is still widely accessible in the form of creams, gels, tablets, and suppositories for local treatment.

Category: - antifungal medications called imidazole

Empirical formula: - $C_{18}H_{14}Cl_4N_2O$

Chemical structure: –

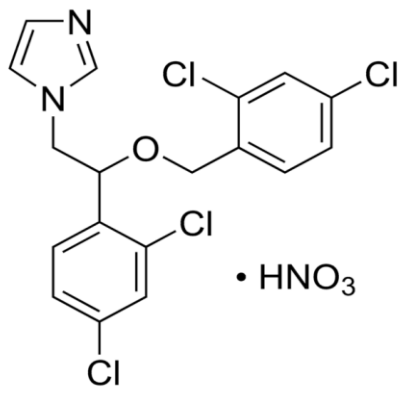

Fig 1.8: - Structure of Miconazole nitrate

Molecular weight: - 416.1 g/mol

Chemical name: - 1-[2-(2,4-Dichlorophenyl)-2-[(2,4-dichlorophenyl) methoxy]-1H-imidazolomononitrate]

Appearance: - white or off-white crystal or powder

Odour: - mild chemical odour

Melting point: 184 °C

Boiling point: 551.1 °C

Synonyms: - Brentan, Daktarin, miconazole, Miconazole nitrate, Monistat, Monistat IV, Miconozolo, Miconozolum, Minostate

Density: - 1.451g/cm^3

Storage: - Ambient long-term storage (2–8 °C)

Solubility: – Miconazole (nitrate) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of miconazole (nitrate) in ethanol is approximately 0.1 mg/ml and approximately 25 mg/ml in DMSO and DMF.

Mechanism of action: – Miconazole is an azole antifungal used to treat a variety of conditions, including those caused by Candida overgrowth. Unique among the azoles, miconazole is thought to act through three main mechanisms. The primary mechanism of action is through inhibition of the CYP450 14α-lanosterol demethylase enzyme, which results in altered ergosterol production and impaired cell membrane composition and permeability, which in turn leads to cation, phosphate, and low molecular weight protein leakage. In addition, miconazole inhibits fungal peroxidase and catalase while not affecting NADH oxidase activity, leading to increased production of reactive oxygen species (ROS). Increased intracellular ROS leads to downstream pleiotropic effects and eventual apoptosis.[25]

Lastly, likely as a result of lanosterol demethylation inhibition, miconazole causes a rise in intracellular levels of farnesol. This molecule participates in quorum sensing in Candida, preventing the transition from yeast to mycelial forms and thereby the formation of biofilms, which are more resistant to antibiotics. In addition, farnesol is an inhibitor of drug efflux ABC transporters, namely Candida CaCdr1p and CaCdr2p, which may additionally contribute to increased effectiveness of azole drugs.[26]

Pharmacokinetics: -

Absorption: – Topical miconazole is absorbed poorly into the systemic circulation. In paediatric patients aged 1–21 months given multiple topical applications of miconazole ointment for seven days, the plasma miconazole concentration was less than 0.5 ng/mL in 88% of the patients, with the remaining patients having a concentration of 0.57 and 0.58 ng/mL, respectively. Similarly, patients administered with a vaginal 1200 mg ovule had a mean Cmax of 10.71 ng/mL, mean Tmax of 18.4 hours, and mean $AUC_{0–96}$ of 477.3 ng*h/mL.

Distribution: – A 1200 mg miconazole vaginal suppository resulted in a calculated apparent volume of distribution of 95 546 L while a 100 mg vaginal cream yielded an apparent volume of distribution of 10 911L.

Metabolism: – Miconazole is metabolized in the liver and does not give rise to any active metabolites.

Protein binding: – In vitro data suggests that miconazole binds human serum albumin, however, the clinical significance of this observation is unclear.

Excretion: – Miconazole is excreted through both urine and faeces; less than 1% of unchanged miconazole is recovered in urine.

Pharmacodynamics: – Miconazole is an azole antifungal that functions primarily through inhibition of a specific demethylase within the CYP450 complex. As miconazole is typically applied topically and is minimally absorbed into the systemic circulation following application, the majority of patient reactions are limited to hypersensitivity and cases of anaphylaxis. Patients using intravaginal miconazole products are advised not to rely on contraceptives to prevent pregnancy and sexually transmitted infections, as well as not to use tampons concurrently.

Antifungal spectrum: – Miconazole nitrate is a broad-spectrum antifungal that works against:

Yeasts: - Especially Candida (e.g., for thrush and vaginal yeast infections).

Dermatophytes: - Like Trichophyton and Microsporum (e.g., for athlete's foot, ringworm).

Other Fungi: - Such as Malassezia (e.g., for dandruff).[27]

1.8 Excipient profile: -

1. Chitosan: -

Official name: Chitosan

Synonyms: Poly-(β-(1→4)-2-amino-2-deoxy-D-glucopyranose); Deacetylated chitin

Category (functional): Pharmaceutical excipient, Biopolymer**,** Mucoadhesive agent**,** Controlled-release matrix former**,** Drug delivery carrier

Description: Chitosan is a natural cationic polysaccharide obtained by partial deacetylation of chitin, the main structural component of crustacean shells. It appears as a white to off-white, odorless, amorphous powder or flakes. It is insoluble in water and organic solvents but soluble in dilute acids (e.g., acetic acid, hydrochloric acid) due to protonation of amino groups.

Chemical formula: $(C_6H_{11}NO_4)_n$

Chemical structure: -

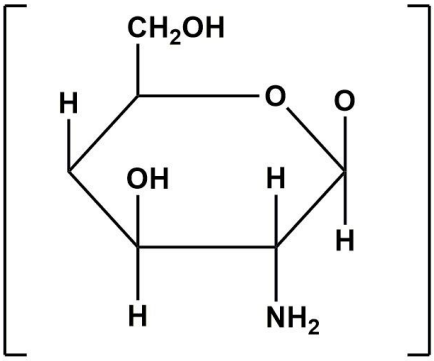

Fig 1.9: - Structure of chitosan

Molecular weight: Varies with degree of polymerization (10–1000 kDa).

Identification: Infrared absorption (characteristic peaks at ~1655 cm^{-1} for amide I and 1595 cm^{-1} for amine).

Degree of deacetylation: typically, ≥70%.

Solubility: Insoluble in water, ethanol, acetone, and most organic solvents. Soluble in dilute aqueous acids such as 1% acetic, formic, or lactic acid.

pH (1% solution): 4.0 – 6.0

Viscosity: Dependent on molecular weight and concentration.

Functional properties: Bio adhesion to mucosal surfaces, Film-forming ability, Biodegradability, Biocompatibility, Antimicrobial activity

Stability and storage conditions: Chitosan is stable at room temperature in dry form. It should be stored in a tightly closed container, protected from moisture and direct light. Aqueous acidic solutions are less stable and may degrade upon prolonged storage.

Incompatibilities: Incompatible with strong oxidizing agents and strong alkalis. It may form complexes with anionic polymers and polyanions (e.g., alginate, sodium lauryl sulfate).

Applications in pharmaceuticals:

- Mucoadhesive polymer in nasal, buccal, ocular, vaginal, and gastrointestinal drug delivery.
- Film and coating agent in tablets and capsules.
- Controlled-release matrix for hydrophilic and hydrophobic drugs.
- Nanoparticle, microsphere, and hydrogel formulation.
- Enhancer of drug absorption by opening tight junctions.

Pharmacological activity:

- Non-toxic and non-immunogenic excipient
- Biodegraded by lysozyme into non-toxic oligosaccharides
- Some intrinsic antimicrobial and hemostatic activity.

2. Glacial acetic acid: -

Drug Profile: Glacial Acetic Acid

Official Name (Pharmacopeia): Acetic Acid Glacial (IP, BP, USP, EP)

Chemical Name: Ethanoic acid

Chemical Formula: CH_3COOH

Chemical structure: -

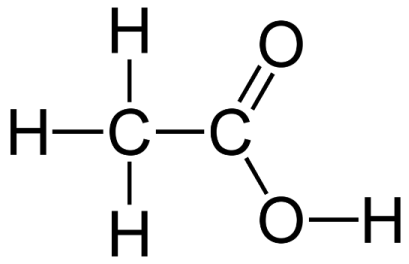

Fig 1.10: - Structure of Glacial acetic acid

Molecular Weight: 60.05 g/mol

Melting point (freezing point): 16.6 – 16.7 °C

Boiling point: 117.9 – 118 °C at 1 atm

Description (Appearance): A clear, colorless liquid**,** Characteristic pungent odor**,** Corrosive to skin and mucous membranes

Identification Tests (Pharmacopeia):

Odor: Pungent, vinegar-like

Solubility: Miscible with water, alcohol, and chloroform

pH: Strongly acidic

Specific Gravity: ~1.049–1.051

Storage: Store in tightly closed containers**,** keep in cool, well-ventilated place, away from metals**,** Protect from light

Pharmaceutical Uses:

- As an acidifying agent in pharmaceutical formulations
- Used in the preparation of acetate salts
- Employed as a solvent or co-solvent in drug formulation
- Used in ionotropic gelation method of chitosan nanoparticle preparation.

3. Sodium Tripolyphosphate

Official Name: Sodium Tripolyphosphate

Synonyms: Pentasodium triphosphate, STPP

Chemical Formula: $Na_5P_3O_{10}$

Chemical structure:

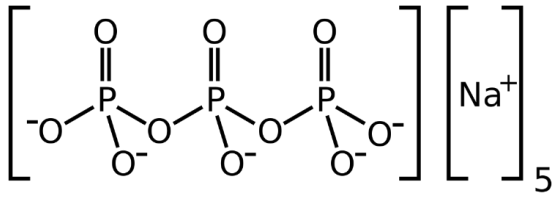

Fig 1.11: - Structure of Sodium Tripolyphosphate

Molecular Weight: 367.86 g/mol

Melting point: about 622 °C

Description: White crystalline powder or granules, Odorless and hygroscopic in nature.

Freely soluble in water; insoluble in ethanol and other organic solvents. Produces alkaline solution in water.

Category:

Excipient (cross-linking agent, stabilizer).

Used in nanoparticle preparation, especially with chitosan, as a polyanionic cross-linker.

Also used in food industry and detergents.

Identification

Infrared spectroscopy (IR): Shows characteristic phosphate group peaks.

Chemical test: Produces white precipitate with silver nitrate after acid hydrolysis (due to phosphate ions).

Storage: -

Store in a well-closed container.

Protect from moisture and direct sunlight.

Hygroscopic – requires desiccated storage conditions.

Applications: -

- Widely used as a cross-linking agent in ionotropic gelation for preparation of chitosan nanoparticles.
- Enhances stability and regulates size of nanoparticles.
- In pharmaceuticals: excipient for controlled drug delivery, stabilizer.

4. Tween 80 (Polysorbate 80)

Official Name: Polysorbate 80

Chemical class: Nonionic surfactant

Molecular formula: C64H124O26 (approximate, due to mixture nature)

Chemical structure:

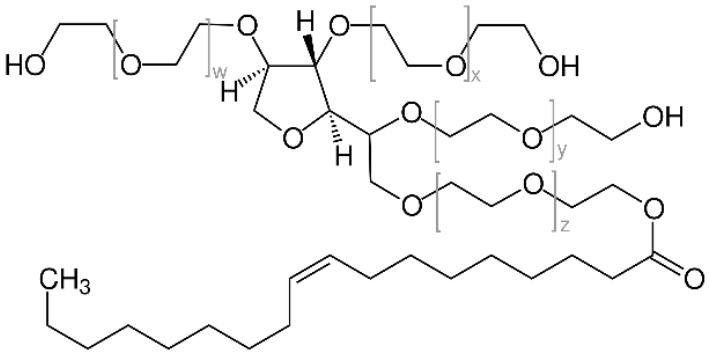

Fig 1.12: - Structure of Tween 80 (Polysorbate 80)

Description: A yellow to amber oily liquid, clear or slightly opalescent, with a faint characteristic odor.

Functional Category: Pharmaceutical excipient**,** Emulsifier, solubilizing agent, dispersing agent, stabilizer, wetting agent

Solubility: Freely soluble in water, ethanol, methanol, ethyl acetate**,** Insoluble in mineral oils

Applications in Pharmaceuticals: -

Used widely as an emulsifying agent in creams, ointments, and lotions

Functions as a solubilizer for poorly soluble drugs (e.g., vitamins, essential oils, antifungals)

Stabilizes suspensions and nanoparticle formulations

Commonly employed in parenteral, oral, and topical preparations

Storage: Store in tight, well-closed containers at room temperature, protected from light and heat

5. Acetone (C_3H_6O): -

Category: Solvent (non-aqueous), excipient

Description: A clear, colorless, highly volatile liquid with a characteristic sweet, fruity odor.

Miscible with water and most organic solvents.

Synonyms: Propanone, Dimethyl ketone

Chemical Formula: C_3H_6O

Chemical structure:

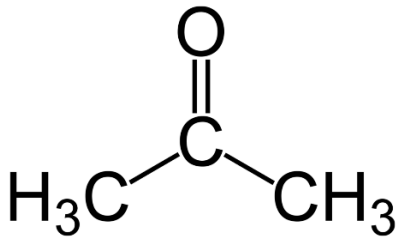

Fig 1.13: - Structure of Acetone

Molecular Weight: 58.08 g/mol

Melting point: −94.7 °C

Boiling point: - 56.1 °C (at 1 atm)

Uses in Pharmaceuticals:

Common solvent in polymeric nanoparticle preparation (e.g., solvent evaporation, nanoprecipitation).

Used in topical and transdermal formulations as a penetration enhancer.

Employed in cleaning laboratory/industrial pharmaceutical equipment.

6. Distilled water: -

Synonyms: Aqua, Hydrogen oxide

Chemical name: Water

Structural formula: (H_2O)

Chemical structure:

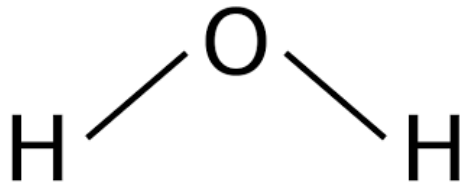

Fig 1.14: - Structure of Water

Functional category: Solvent

Description: The chemical composition of portable water is variable; this portable water is then purified by distillation process in pharmaceutical practices. E.g. Water for injection.

Boiling point: 100 °C

Solubility: Miscible with most solvents.

Specific gravity: 0.9971

Surface tension: 71.97 mN/m

Vapour pressure: 3.17 kPa

Viscosity: 0.889 mPa·s

storage conditions: Water is stable in physical states.

Applications: Purified water is the most widely used excipients in pharmaceutical production operations. Purified water and water for injection are used for cleaning operation and in formulation of various products.

2. AIMS AND OBJECTIVES

2.1 Aim

The main aim of this work is to prepare and evaluate a nanoparticle-based gel containing miconazole nitrate for effective topical antifungal therapy.

2.2 Objectives

The key objectives of the study are:

- Pre-formulation studies conducted for miconazole nitrate drug.
- Pre-formulation studies conducted to select the suitable excipients to develop the dosage form based on properties of drug and Excipients.
- To formulate miconazole nitrate–loaded nanoparticles using suitable excipients.
- To develop a stable topical gel by incorporating the optimized nanoparticles.
- To evaluate the nanoparticle gel

2.3 Need of the Study

Fungal infections often require long treatment durations, but conventional gels and creams have limitations such as poor drug penetration, rapid removal from the skin, and reduced effectiveness. Miconazole nitrate, being poorly soluble in water, shows low bioavailability when applied in

traditional formulations. By loading the drug into nanoparticles, its solubility and stability can be improved, allowing deeper penetration into skin layers and sustained drug release. Incorporating these nanoparticles into a gel base further enhances patient convenience, improves spreadability, and provides better retention at the site of infection. Overall, a miconazole nitrate nanoparticle gel is expected to deliver improved antifungal efficacy, prolonged action, and greater patient acceptability compared to conventional formulations.

4. METHODOLOGY

The chemicals that were used are AR/LR grade or the best possible grade available were used as supplied by manufacturer without further purification or investigation.

Chemical`s list

Table no 1: List of chemicals

Sl.no	Materials	Source
1	Chitosan	Kemphasol, Mumbai
2	Miconazole	Sisco Research Laboratories pvt ltd
3	Glacial Acetic Acid	Thomas Baker (Chemicals) Pvt Ltd, Ambernath
4	Sodium Tripolyphosphate	Kemphasol, Mumbai
5	Tween 80	Molychem, Mumbai
6	Distilled Water	Spurthy College Of Pharmacy
7	Acetone	s d fine chem limited, Mumbai
8	Carbopol 934	Molychem, Mumbai

Equipment's list

Table no 2: List of equipment's

Sl.no	Equipment's	Model/Company
1	Electronic Balance	Systronics, Gujarat
2	UV Spectrophotometer	Jasco Int.co.Ltd, Japan
3	FT-IR Spectrophotometer	Jasco.lnt.co, Ltd, Japan
4	Centrifuge	Rotek Kerala
5	Magnetic stirrer	REMI Electrotechnics ltd., Mumbai, India
6	Digital pH meter	Aczet Pvt, Ltd
7	Digital Microscope	Magnus
8	Viscometer	Brookfield DV-II+Pro
9	Zeta meter	zetaatrac

4.1 Pre-Formulation Studies of Miconazole Nitrate:[29]

Preformulation studies are defined as the investigation of physicochemical properties of the drug. It is a phase which is initiated once the new molecule is seeded. In a broader way, it according with the studies of physical, chemical, analytical and pharmaceutical properties related to molecule and provides idea about suitable modification in molecule to show a better performance.

Objective of the Preformulation study is to develop and design the stable, effective and safe dosage form by obtaining kinetic rate profile, compatibility with the other ingredients and

establish physicochemical parameters of new drug substances.

1. Organoleptic properties

Organoleptic properties like colour, odour and its crystalline property were determined visually.

2. Solubility of miconazole nitrate:[30]

The solubility of miconazole nitrate was performed in various solvent like, water, ethanol, methanol and DMSO Accurately 10mg of drug was transferred in a close and dry test tube and dissolved in 1ml of the solvents individually and shakes vigorously and the solubility of the drug was checked visually.

3. Melting point determination of miconazole nitrate:[40]

The melting point of miconazole nitrate was determined by using Thiele's tube method by taking a small amount of drug in a capillary tube closed at one end and placed in Thiele's tube containing liquid paraffin and temperature at which drug melts was recorded. This was performed in triplicates and the average value was reported.

4. Differential Scanning Calorimetry (DSC):[31]

Differential Scanning Calorimetry (DSC) is a thermo analytical technique in which the difference in the amount of heat required to increase the temperature of a sample and reference are measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature throughout the experiment DSC experiments were carried out in order to characterize the physical state of the drugs. Samples of formulation were placed in aluminium pans and thematically sealed. The heating rate was 20°C per minute using nitrogen as the purge gas. The DSC instrument was calibrated for temperature using Indium. In addition, for enthalpy calibration Indium was sealed in aluminium pans with sealed empty pan as a reference.

5. Ultraviolet Spectrum:[32]

Miconazole nitrate solution was prepared in 7.4 pH and diluted suitably. The UV spectrum of the solution was taken on UV Shimadzu 1800 UV/Vis double beam spectrophotometer. The value was compared with the standard value.

6. Infrared Spectral studies:[33]

Method: Approximately 1 mg of the miconazole nitrate was allowed to mix with about 100 mg of KBr (which is transparent to IR) in the ratio of 1:100. Thoroughly mix in a mortar. The mixture was pressed into a pellet die manually. Place it in Fourier Transform Infrared (FTIR) Spectrophotometer

7. Preparation of standard graph of miconazole nitrate:[34]

Procedure:

a) Preparation of Standard solution of miconazole nitrate (7.4 pH phosphate buffer)

1st Stock:100mg of miconazole nitrate was accurately weighed into a 100ml volumetric flask and dissolved in a small quantity of methanol and volume was made up to 100 ml using phosphate buffer 7.4 pH (1mg/ml or 1000µg/ml)

2nd Stock:1ml of the above solution was pipette into another 10 ml in volumetric flask. Volume was made up to 10 ml with buffer (0.01mg/ml or 100µg/ml). From the standard solution of 2nd stock pipette 0.5ml, 1ml, 1.5ml, 2ml and 2.5ml into 10 ml volumetric flasks respectively. Make up

the volume with buffer to get 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml and 25µg/ml respectively.

The spectrum of this solution was run in a 200-400nm range in UV-Visible Spectrophotometer. The absorbance of each concentration was measured at 229nm using buffer as blank this was performed in triplicates and the average value was reported.

b) Preparation of Standard solution (pH 7.4-Phosphate buffer)

Weigh accurately 2.38gm of disodium hydrogen phosphate in small amount of distilled water and shake well till it solubilizes completely to the above solution add 0.19gm of dihydrogen phosphate and mix well till it solubilizes add 8gm of sodium chloride to the above solution and make up the volume to 1000ml. Shake until the solutes are completely solubilized. Filter the above solution using a whatmann filter paper

8. drug-polymer/excipient compatibility:[35,41]

FTIR spectrophotometer:

The compatibility of drug and polymer was analysed using FTIR spectrophotometer in this technique, 1mg of the sample and 100mg of potassium bromide (KBr) (1:100 ratio) was finely ground using mortar and pestle. A few mixtures were placed for 2 minutes under a hydraulic press compressed at 7kg/cm² to form a transparent pellet. The pellet was kept in the sample holder and scanned from 4000 cm^{-1} to 400 cm^{-1} in Shimadzu FTIR spectrophotometer. Samples were prepared for the drug, polymer and physical mixture of drug and polymers. The spectra obtained were compared and interpreted for the functional group peaks.

4.2 Preparation Of Chitosan Nanoparticle: [36]

MATERIALS:

1. Chitosan
2. Miconazole
3. Glacial acetic acid
4. Sodium tri poly phosphate
5. Tween 80
6. Distilled water
7. Acetone

Formulation Code for Chitosan– Miconazole Nanoparticle: -

Table no 3: Formulation Chart for Chitosan– Miconazole Nanoparticle

Formulation Code	Chitosan (mg)	Acetic Acid (1% v/v) (ml)	Miconozole (mg)	Acetone/ Ethanol (ml)	TPP Solution (0.5mg/ml) (v/v)	Tween 80 in TPP Soln (%w/v)
F_1	50	20	2.5	0.2	5	0
F_2	50	20	2.5	0.2	7	0
F_3	75	20	2.5	0.3	7	0.1
F_4	75	20	2.5	0.3	9	0.1

1. **Preparation of Chitosan solution: -**

- Weigh required amount of chitosan.

- Slowly add it to 20ml of 1% v/v Acetic acid Solution. (Prepared by diluting 1ml glacial acetic acid with distilled water to 100ml).
- Stirr it at temperature of 70°C until the chitosan dissolves
- Chitosan solution is prepared.

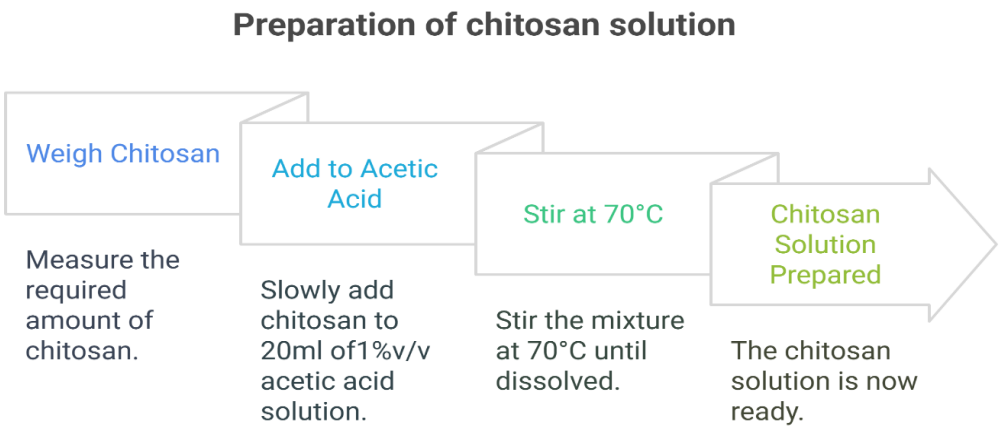

Fig 4.1: - Preparation of chitosan solution

2. Preparation Of Miconazole Stock Solution: -

- Weigh miconazole of about 2.5 mg.
- Dissolve it in Acetone or Ethanol.
- Miconazole solution is prepared.

Fig 4.2: - Preparation of miconazole stock solution

3. **Preparation of Sodium Tripolyphosphate solution: -**

- 50mg of sodium tripolyphosphate in 100ml of distilled water.
- Stir it properly so it gets dissolves.
- Sodium Tripolyphosphate solution is prepared.

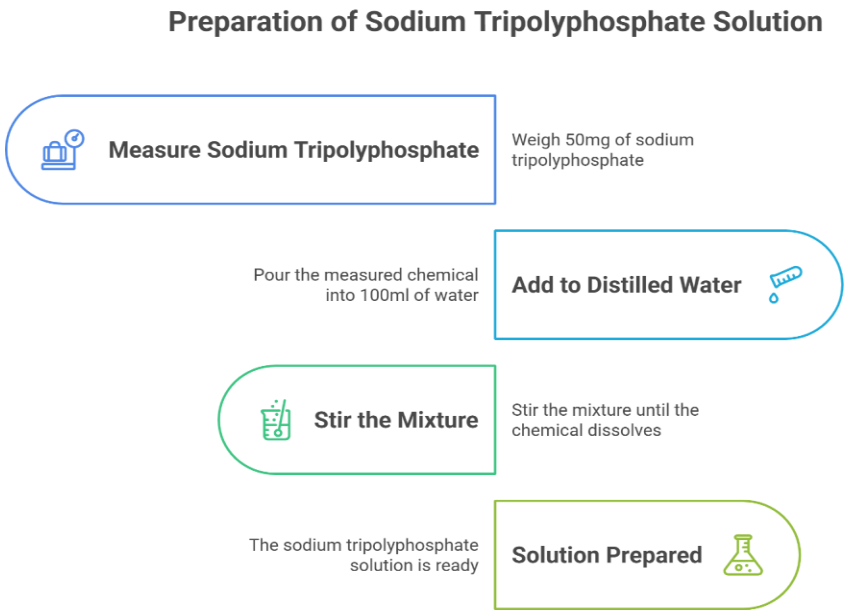

Fig 4.3: - Preparation of STPP solution

4. **Tween 80 Formulation: - (For F3 and F4)**

- Required amount of Tween 80 is measured and for that above STTP Solution is added.
- Dissolve it in 0.1 gm for 100ml TPP solution to make 0.1 % w/v.

Nanoparticle synthesis: -

1. **Combine Chitosan solution and Miconazole solution: -**

- Add prepared miconazole stock solution into chitosan solution.
- Then Stir it for 30 mins at room temperature.
- Miconazole dispersed chitosan solution has obtained.

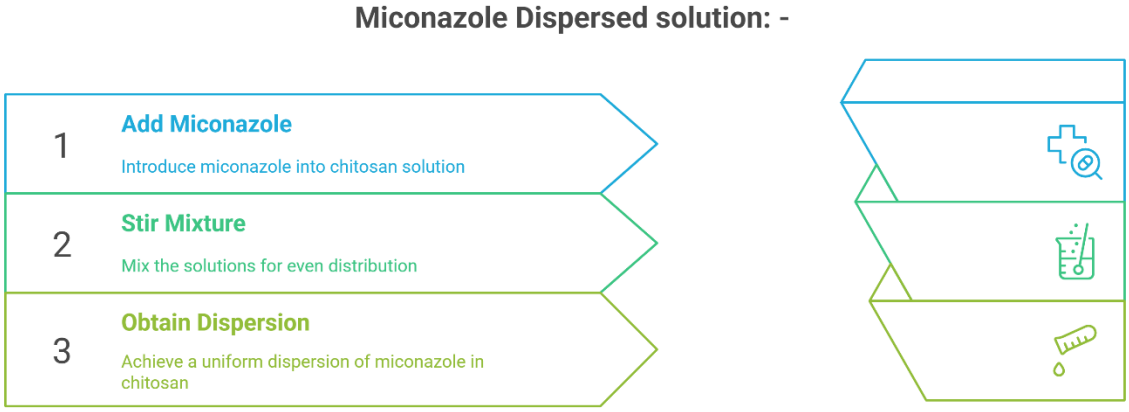

Fig 4.4: - Preparation of miconazole dispersed solution

2. Ion Chelation: -

- Chitosan – Miconazole solution is kept under magnetic stirrer.
- Further TPP solution is added slowly by using Syringe at dropwise (0.5 ml to 1ml/ min).
- Stir it for 2 hours.
- Then Particle stabilization and complete reaction occur.

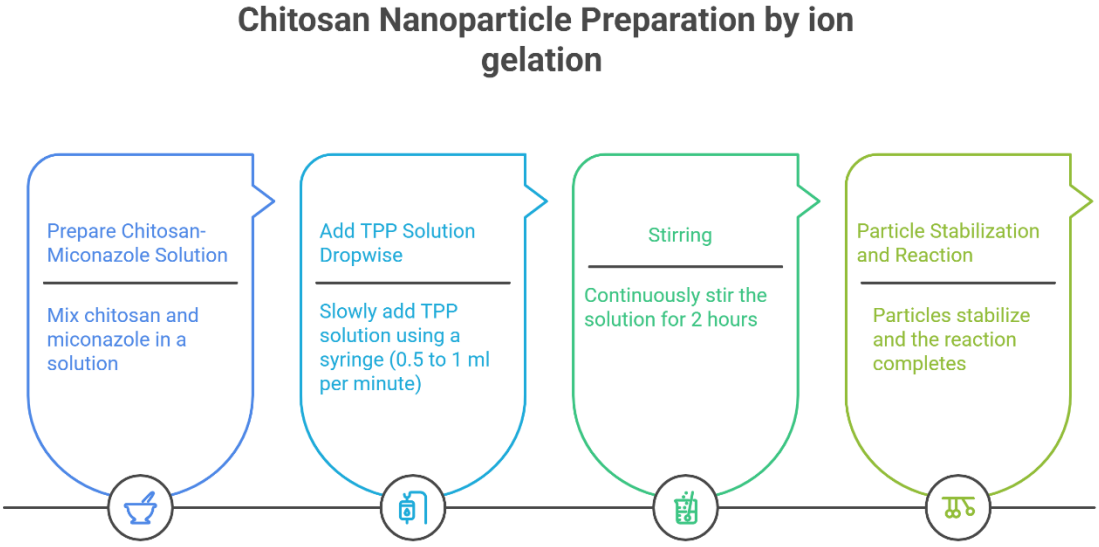

Fig 4.5: - Preparation of chitosan nanoparticle by ion gelation

4.3 Evalution Of Nanoparticle: -

1. Physical inspection
2. Particle size
3. Zeta potential
4. Percentage drug entrapment efficiency (%)
5. MORPHOLOGY

- Scanning Electron Microscope (SEM)

Physical Inspection:[44,45]

The physical appearance of the prepared nanoparticle dispersion was observed visually.

Particle size [43]

The particle size of the optimized nanogel was measured using malvern zetasizer.

Zeta potential [37]

Zeta potential determines the stability of the formulation by measuring the charge of the drug-loaded droplet surface. Zeta potential for the optimized batch was measured using Malvern Zetasizer. For the determination of zeta potential, nanoparticles were diluted with 0.1 mM KCl and placed in the electrophoretic cell with15 V/cm electric field.

Percentage drug entrapment efficiency (%)[28]

1 ml of nanoparticle sample is taken for centrifugation at 7168 RCF (relative centrifugal force) for 50 min. The supernatant was collected, washed, and filtered through membrane (0.45 micron) filter paper. The absorbance of the sample was noted, and the actual entrapped drug was calculated using the below-mentioned formula: The readings were taken in triplicate.

$$Total\ drug\ concentration\ = \frac{Total\ amount\ of\ drug - Amount\ of\ drug\ in\ supernatant}{Total\ amount\ of\ drug} X100$$

Morphology

Scanning Electron Microscope (SEM) [28,46]

The morphology (shape and surface characteristics) of NLC was studied by scanning electron microscopy (SEM) (model JSM 840A, JEOL, Japan). The sputtering was done for nearly 5 minutes to obtain uniform coating on the sample to enable good quality SEM images. The SEM was operated at low accelerating voltage of about 15KV with load current of about 80MA.

4.4 Preparation Of Chitosan Nanoparticle Gel:

Materials:

- Chitosan nanoparticle suspension
- Tri ethanol amine
- Carbopol 934
- Distilled water

Formulation chart for log batch of nanogel: -

Table no 4: - Formulation Chart for log batch of Nanogel

Formulation code	Nanoparticle suspension (from optimal nanoparticle batch)	Carbopol 934 (% w/v)	Distilled water (in ml)	Triethanol amine (drops)
G_1	2 ml (containing 2.5 mg of MCZ)	0.5	q. s	q. s
G_2	2 ml (containing 2.5 mg of MCZ)	0.75	q. s	q. s
G_3	2 ml (containing 2.5 mg of MCZ)	1.0	q. s	q. s

1.Hydrate Carbopol for gel base

Weigh specified amount of Carbopol 934

(0.05g for G_1, 0.075g for G_2, 0.1g for G_3)

↓

Slowly sprinkle Carbopol powder on to the surface of

distilled water (15 to 20 ml of water for hydration) in a beaker

↓ 4- 6 hrs

↓ →

Allow to hydrate prevent lump formation

↓

After hydration, stirr until a clean, homogenised

Dispersion is obtained

↓

GEL BASE

2.Incorporation of nanoparticle suspension

Add the chitosan -MCZ nanoparticle suspension to the

Carbopol gel base (slowly)

↓ stirr

Uniform mixing of nanoparticle

↓

Add additional distilled water to bring the total weight

less than 10 g (approx. 9.5g)

↓

Add TEA drop wise to the mixture (PH 6.0-6.5)

↓ Stirr for 15-20 mins

Homogenise and complete formulation by adding

water to make up the weight to 10g

↓

Nanogel containing miconazole nitrate

nanoparticles was obtained

NOTE: As the PH increases, the Carbopol will swell rapidly and the viscosity will increase forming a clean gel

4.5 Evolution of Nanogel: -

1. Visual inspection
2. PH determination
3. Viscosity
4. Spreadability
5. Drug content uniformity (UV-vis spectroscopy)

Visual inspection 38

Miconazole nanogel underwent visual inspection to assess their uniformity, texture, absence of phase separation, and any signs of aggregation.

PH determination 39

A specific quantity of gel, measured in grammes, was precisely weighed and subsequently dispersed in 25 ml of distilled water. pH of dispersion was determined using a digital pH meter.

Viscosity28

The viscosity of prepared gel was measured using Brookfield viscometer at different RPM viscosity was measured and noted. The measurement was made over the whole range of speed settings from 5-100 rpm with 10 seconds between two successive speeds.

Spreadability28

The Spreadability of the gel formulation was determined by using sliding plate apparatus and by measuring the diameter of 1 gm of gel between horizontal plates after 1 minute. The standardized weight tied on the upper plate was 20 gm. An excess of gel is placed between two glass slides and a 1000 gm weight is placed on them for 5 minutes, to compress the sample to a uniform thickness. The bottom slide is anchored to the apparatus and weights are placed in the pan. The time in seconds needed to separate the two slides is taken as a measure of spreadability. A shorter time interval indicates better spreadability. Spreadability was determined by using the following formula.

Spreadability(S)= (M×L)/T X 100

Where,

M = weight tied to the upper slide.

L = length of the glass slide.

T = Time taken to separate two slides (sec).

Drug content uniformity (UV-vis spectroscopy)[28]

1 gm of gel which was quantity equivalent to the dose of the drug was dissolved in 100 ml of phosphate buffer pH 6.8. A sample (5 ml) was taken from this solution and diluted to 25 ml, then Miconazole Nitrate concentration was determined by measuring the absorbance at 272 nm using UV-visible Spectrophotometer.

$$\%\ of\ drug\ content\ = \frac{\text{Amount of drug obtained after centrifugation}}{\text{Amount of drug taken}}\ X\ 100$$

5. RESULTS

5.1 pre formulation studies

1. Determination of Organoleptic characters

The Organoleptic characters like colour odour and state for the given drug sample was studied.

Table no 5: - Organoleptic test

Colour	White to pale cream
Odour	Odourless/almost odourless
State	Crystalline or micro crystalline powder

2. Determination of Solubility

Table no 6: - Solubility profile of miconazole nitrat

Medium	Solubility
Water	Insoluble
Methanol	Soluble
Ethanol	Soluble
DMSO	Soluble

3. Determination of Melting point

Table no 7: - Melting point of miconazole nitrate

Drug Name	Observed melting point	Standard melting point
Miconazole nitrate	180±1°C	179- 184°C

Differential scanning Calorimetry of miconazole nitrate

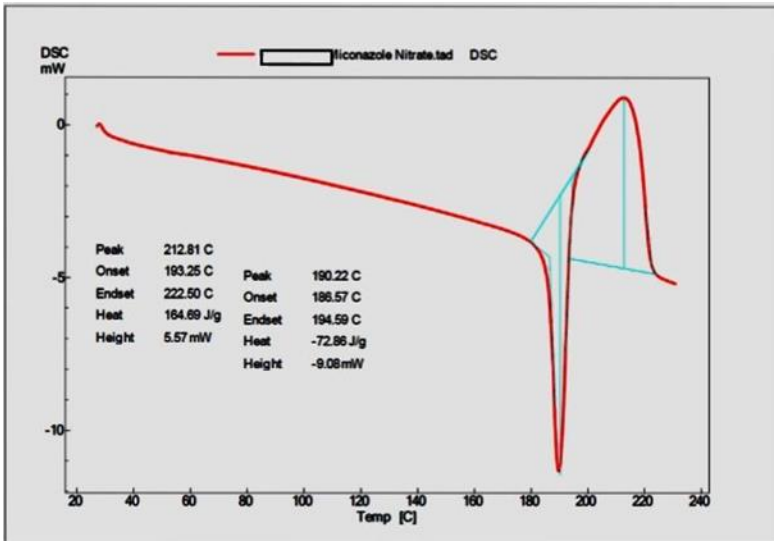

Figure 5.1: DSC of miconazole nitrate

Determination of λmax of Drug by UV spectrophotometer:

Table no 8: - λ-max of Miconazole Nitrate

Drug Name	Observed λmax (nm)	Standard λmax (nm)
Miconazole nitrate	272	272

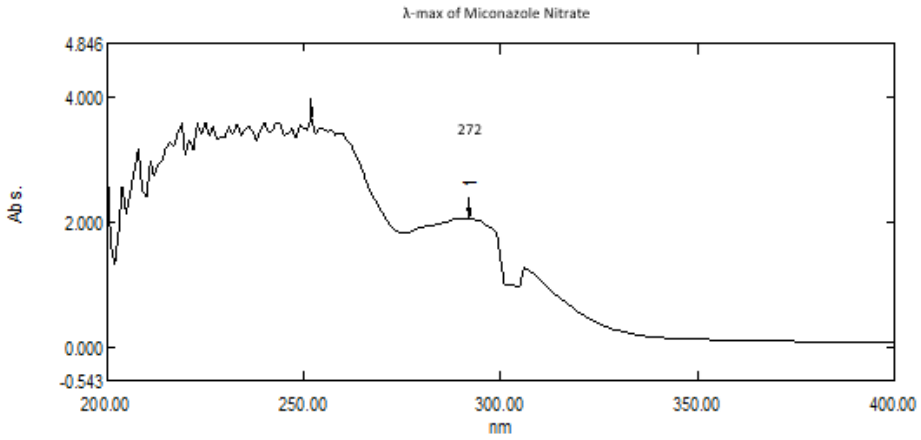

Figure 5.2: λ-max of Miconazole Nitrate

6. IR Spectrum of miconazole nitrate

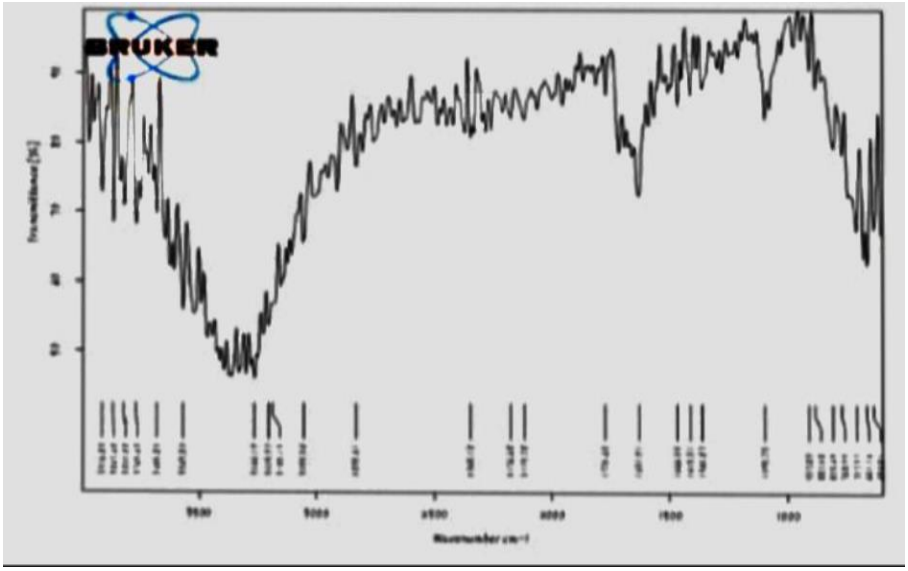

Figure 5.3: IR spectrum of miconazole nitrate

7. Calibration curve of Miconazole nitrate

Table no 9: - Calibration curve of miconazole nitrate

Sl no.	Concentration of Miconazole nitrate (mg)	Absorbance
01	0	0±0
02	5	0.05±0.01
03	10	0.11±0.01
04	15	0.16±0.01
05	20	0.21±0.02
06	25	0.25±0.01
07	30	0.3±0.05

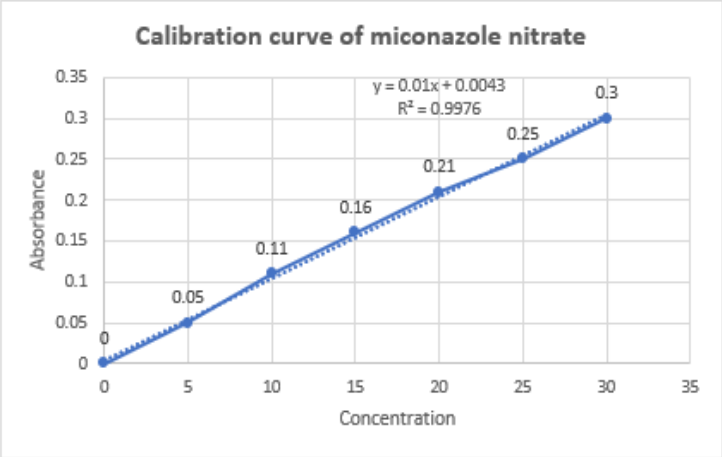

Figure 5.4: Calibration curve of miconazole nitrate

8. Drug- Excipient Compatibility The FTIR was done for drug with excipients

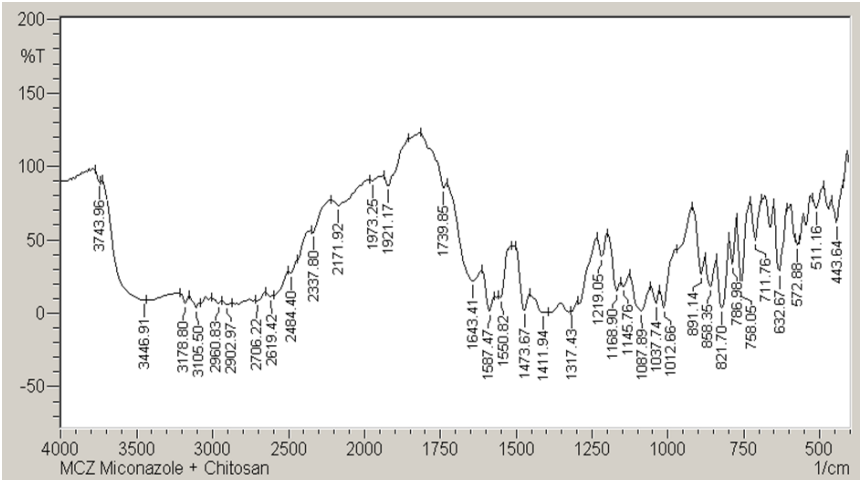

Figure 5.5: FTIR of MCZ+ Chitosan

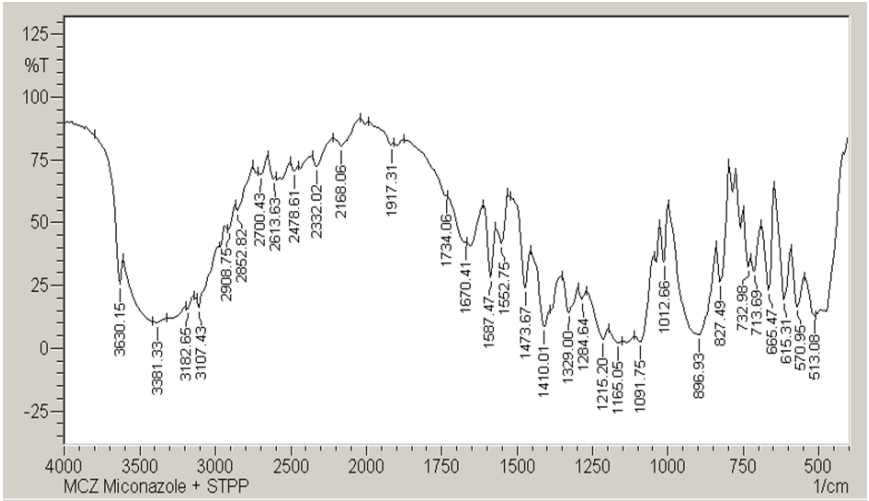

Figure 5.6: FTIR of MCZ+ STPP

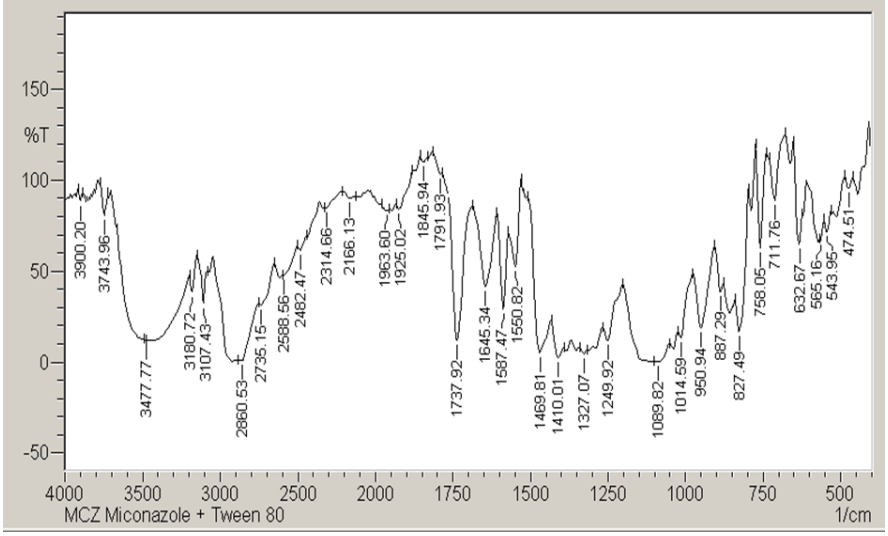

Figure 5.7: FTIR of MCZ+ Tween 80

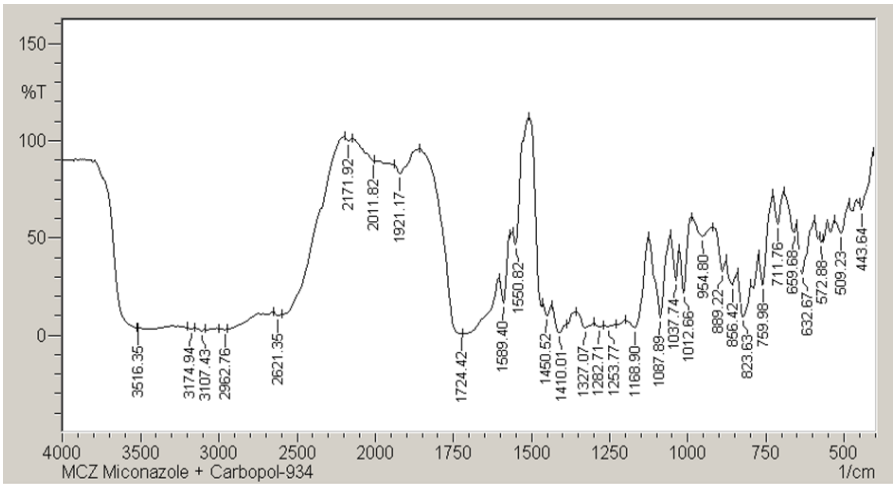

Figure 5.8: FTIR of MCZ+ Carbopol-934

Table no 10: - Comparison of FT- IR spectra of MCN and polymer

Sl. No	Functional Group	Reported Frequency (cm^{-1})	Observed in MCZ (cm^{-1})	With Chitosan	With Carbopol 934	With STPP	With Tween 80	Remarks
1	O–H / N–H Stretch	3200–3500	3446	3446, 3178	3516, 3174	3381, 3182	3477, 3180	Broadening with excipients (H-bonding)
2	C–H (Aliphatic)	2850–2950	2920, 2852	2920, 2850	2926	2908, 2852	2860, 2936	Slight shifts
3	Aromatic C–H	~3050	3050–3070	3060	3071	3071	3107	Retained
4	C=N (Imidazole ring)	1500–1600	1588, 1508	1597, 1550	1589, 1550	1587, 1562	1587, 1550	No significant change
5	C–N Stretch	~1450	1452	1417, 1451	1410, 1450	1410	1469, 1410	Retained

6	C–O Stretch	1050–1250	1225, 1110	1219, 1169, 1087	1253, 1169, 1083	1215, 1165, 1091	1249, 1089, 1014	Minor shifts only
7	C=O (Excipient ester / Carbopol)	~1730–1740	–	1739	1724	1734	1737	Attributed to excipients
8	C–Cl bending	<800	750, 690	756–632	759–632	732–666	758–632	Retained

5.2 Evaluation of Miconazole Nanoparticle Dispersion

Physical Inspection

The physical examination was caried out for the dispersions

Table no 11: - Physical inspection of Nanoparticle dispersion

Formulation code	Transparency / Opacity	Homogeneity	Clumping
F_1	Slightly translucent	Uniform	No clumping
F_2	Slightly translucent	Homogeneous	No clumping
F_3	Slightly translucent	Uniform	No clumping
F_4	Slightly translucent	Uniform	No clumping

Particle size

Table no 12: - Particle size of F_2

Formulation code	Particle size
F_2	235nm

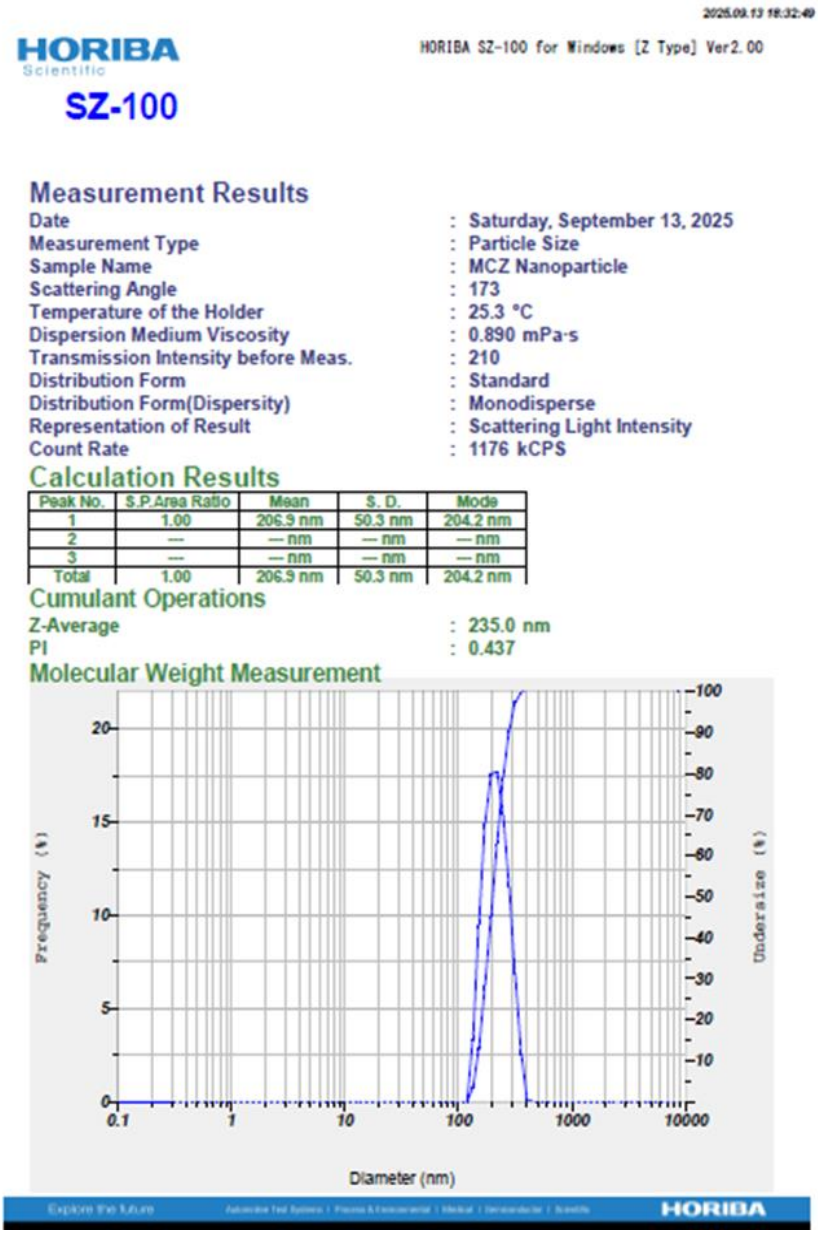

Figure 5.9: Particle size of F_2

Zeta potential

Table no 13: - Zeta potential of F_2

Formulation code	Zeta potential
F_2	-27.0mV

2026.09.13 21:57:21

HORIBA Scientific

HORIBA SZ-100 for Windows [Z Type] Ver2.00

SZ-100

Measurement Results

Measurement Results

Date	:	Saturday, September 13, 2025 9:56:49 PM
Measurement Type	:	Zeta Potential
Sample Name	:	MCZ Nanoparticle Dispersion 13 09 25 zeta
Temperature of the Holder	:	25.3 °C
Dispersion Medium Viscosity	:	0.890 mPa·s
Conductivity	:	0.132 mS/cm
Electrode Voltage	:	3.4 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-27.0 mV	-0.000210 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -27.0 mV

Electrophoretic Mobility Mean : -0.000210 cm²/Vs

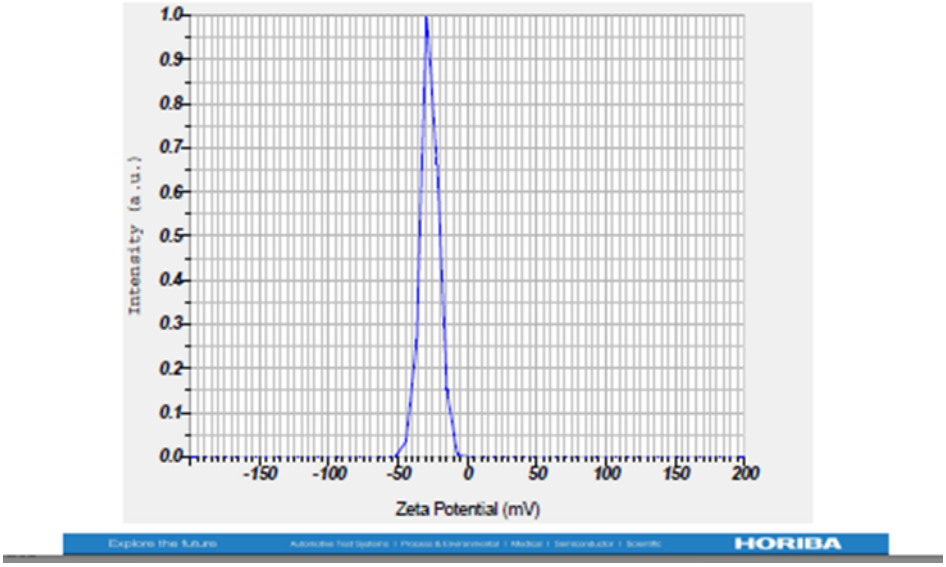

Figure 5.10: Zeta potential of F_2

Drug entrapment efficiency (%)

Table no 14: - Percentage entrapment efficiency

Sl No	Formulation code	Percentage Entrapment Efficiency (%)
1	F_1	95.12%
2	F_2	98.81%
3	F_3	94.93%
4	F_4	94.55%

Morphology

Scanning Electron Microscope (SEM)

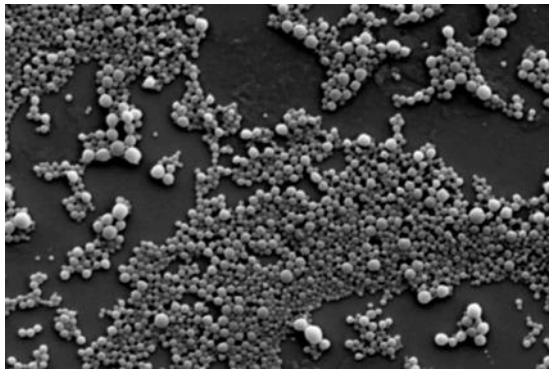

Figure 5.11: Scanning Electron Microscope (SEM) of F_2

5.3 Evaluation of Miconazole Nitrate Loaded Nanogel:

The prepared Nanogel was visually inspected for parameters listed in table

1.Visual inspection

Table no 15: - Visual inspection of prepared nanogel

Formulation code	Colour	Clarity	Consistency	Presence of particulates
F_1	off-white	clear	smooth	Not present
F_2	off-white	clear	smooth	Not present
F_3	off-white	clear	granular	Not present
F_4	off-white	clear	smooth	Not present

2.pH determination

Table no 16: - pH of prepared nanogel

Formulation	pH
F_1	4.76
F_2	4.98
F_3	3.92
F_4	4.12

3.Viscosity

Table no 17: - Viscosity of prepared nonogel

Formulation	Viscosity (m.pa.s)
F_1	10001
F_2	10041
F_3	9711
F_4	9986

4.Spreadability

Table no 18: - Spreadability of prepared nonogel

Formulation	Spreadability(g·cm/s)
F_1	5.6
F_2	5.4
F_3	5.6
F_4	8.0

5.Drug content (UV-vis spectroscopy)

Table no 19: - %Drug content

Sl No	Formulation	%Drug content
1	F_1	91.53%
2	F_2	94.98%
3	F_3	88.36%
4	F4	90.18%

6. DISCUSSION

The present study focuses on the formulation and evaluation of a miconazole nitrate loaded nanoparticle gel to enhance skin penetration and improve drug bioavailability. Miconazole nitrate is a broad-spectrum antifungal agent that acts by inhibiting ergosterol biosynthesis and peroxidase activity, resulting in the accumulation of toxic peroxides and subsequent fungal cell death.

Topical drug delivery systems provide several advantages, including localized action, avoidance of first-pass metabolism, improved patient compliance, and reduced systemic side effects. The skin, being the largest organ of the body, serves as a major barrier influencing drug permeation. Its structure—particularly the stratum corneum, hair follicles, and pores—plays a crucial role in determining the extent and rate of drug absorption, favouring lipophilic compounds.

Thus, nanoparticle gel-based formulations of miconazole nitrate offer a promising approach to overcome the skin barrier, enhance drug penetration, and provide effective treatment for superficial fungal infections like dermatophytosis, superficial candidiasis, and pityriasis versicolor with improved therapeutic outcomes.

6.1 Preformulation studies

1. Organoleptic characters: -MCZ's organoleptic characteristics, such as general description, colour, odour and state were studied. MCZ was discovered to be a white crystalline powder that is somewhat bitter, odourless, and falls within the published literature limitations. Table no. 5 displays the results observed.

2. Determination of solubility:

The solubility of miconazole nitrate showed that it was soluble in methanol, DMSO, ethanol and insoluble in water as shown in table No. 6

3. Determination of melting point:

The melting point of miconazole nitrate was determined by Thiele's tube method, and it was found to be 180±1°C. The value obtained is within the standard range of value of 184°C (table no. 7)

4. Differential scanning calorimetry (DSC) of drug:

DSC thermogram showed a sharp endothermic peak at 184±°C which is corresponding to the melting point of the drug (Fig 5.1). This value was found to near the standard range of 184°C. Thus, the presence of miconazole nitrate was confirmed.

5. Determination of λmax by UV Spectrophotometer:

Between 200 and 400 nm, the absorption spectra of pure Miconazole Nitrate was scanned. In methanol, the λ-Max of pure MCZ was determined to be 272 Nm. Fig 5.2 depicts the results achieved.

6. IR spectroscopy of drug:

The IR spectrum of miconazole nitrate was recorded by FT-IR spectrophotometer as Shown in (Fig. 5.3). From the peaks observed, it was seen that the functional group Peak frequencies were in resemblance to the standard range values of Miconazole Nitrate. Thus, the presence of miconazole nitrate can be confirmed.

7. Standard calibration curve of Miconazole nitrate

Miconazole Nitrate calibration curve was obtained at a wavelength of 272 nm in the Concentration range of 5-30 g/ml. It exhibits high linearity, as illustrated in fig.5.4, with a regression coefficient of 0.9976 (r2 value)

8. FTIR (Drug and excipient compatibility)

All major functional peaks of Miconazole were retained in mixtures with Chitosan, Carbopol 934, STPP, and Tween 80. Minor shifts and broadening were observed in the O–H/N–H region (3200–3500 cm^{-1}), indicating possible hydrogen bonding with polymeric excipients. Characteristic imidazole C=N, C–Cl, and aromatic peaks of Miconazole remained unchanged, confirming no chemical interaction. New peaks at ~1730 cm^{-1} correspond to C=O stretching of excipients (Carbopol, Tween, STPP). Overall, the study confirms compatibility of Miconazole with Chitosan, Carbopol 934, STPP, and Tween 80, suitable for formulation development.

6.2 Evaluation of Nanoparticle dispersion

1. Physical examination

Miconazole Nitrate nanoparticle dispersions were produced in a uniform and homogeneous appearance. The formulations were slightly translucent with no clumping in it. The outcomes were recorded in Table No. 11

2. Particle size

The particle size determination was done for the optimized batch and the size was within the nano range that is 235nm as shown in Fig 5.9

3. zeta potential

The zeta potential was determined for the optimized batch and the zeta potential was shown in 27.0mV as shown in Fig 5.9

4. Drug entrapment efficiency (%)

The drug entrapment efficiency (%) of the nanoparticle dispersion was determined by spectrophotometry at 272 nm, with drug entrapment efficiency ranging from 94.55% to 98.81% percent. The highest drug entrapment efficiency (%) was found with F2 (98.81 %). The results were shown in the table No.14.

5. Scanning electron microscopy

The surface morphology was studied using SEM. SEM photograph Fig 5.11 showed that nanoparticles formed were nearly spherical and homogeneous

5.3 Evaluation Of Miconazole Nitrate Loaded Nanogel:

1. Visual inspection

Miconazole Nitrate nanoparticle gel was produced in an off-white colour with a smooth, homogeneous consistency. The formulations were clear and no particulates were present. The outcomes were shown in table No.15.

Fig 5.12 depicts the prepared nanogels and Fig 5.13 Represents the best formulations.

1. pH

The pH of the formulation was measured by the digital pH meter the pH of the optimised F_2 nanogel is found to be 4.98 as mentioned in table no.16

2. Viscosity

Viscosity of the nanogel is measured, it measured by Brookfield viscometer the viscosity of the nanogel is found to be 10042 as mentioned in table no.17

3. Spreadability

The Spreadability of the F_2 formulation was found to be 5.4 g.cm/s as mentioned in the table no.18

4. Drug content

The drug content of nanogel was determined by spectrophotometry at 272 nm, with drug concentrations ranging from 88.36% to 94.98%. The highest drug content was found with F2 (94.98 %). The results were shown in the table No.19

7. CONCLUSION

Based on the results the evaluation parameter it can be concluded that.

1. The pre-formulation studies involving solubility, melting point, λ-max and DSC determination of the drug was found to be comparable with the standard.

2. Infrared spectroscopy indicates that the drug is compatible with the excipients.

3. Nanoparticle Formulation F2 showed the good results in drug entrapment efficiency, zeta potential, scanning electron microscopy and Particle size

4. The formulation was stable, homogeneous, and showed excellent consistency without any clumps Hence the above result we conclude that it is

possible to formulate Miconazole Nitrate Nanoparticles for topical use.

5. The prepared Miconazole nitrate Nanoparticle F_2 was incorporated into G_3 gel base and miconazole nitrate loaded nanoparticle gel was formulated which was evaluated for pH, viscosity, spreadability and drug content.

8. Summary

The present study was undertaken with an aim to Formulate and Evaluate the nanoparticle gel Containing Miconazole Nitrate to enhance the solubility, bioavailability, and effectiveness of Miconazole Nitrate for topical use.

The identification of the drug was done using Solubility, Melting point, UV-Visible, FTIR and DSC. All the analysis successfully confirmed the identity of the drug (Miconazole nitrate). The drug excipients compatibility was performed using FTIR. FTIR results showed that the drug (Miconazole nitrate) was compatible with the surfactant, polymer, sodium tripolyphosphate.

Various tests, including physical evaluation, particle size, zeta potential and drug entrapment efficiency, were performed. The formulation was stable, homogeneous, and showed excellent consistency without clumping

The optimized formulation F2 leads to formation of nanogel and it evaluated for visual inspection, pH, Viscosity, Spreadability and Drug content The formulation results were within the prescribed limit.

Hence, From the above obtained data it can be summarized that it possible to formulate the Miconazole nitrate loaded nanoparticle gel which enhances the bioavailability by improving the solubility and skin penetration that is important for treating superficial fungal infections like dermatophytosis, superficial candidiasis, and pityriasis versicolor with improved therapeutic outcomes.

REFERENCES

1. Zhao L, Chen J, Bai B, Song G, Zhang J, Yu H, Huang S, Wang Z, Lu G. Topical drug delivery strategies for enhancing drug effectiveness by skin barriers, drug delivery systems and individualized dosing. Front Pharmacol. 2024 Jan 16; 14:1333986.
2. Raina N, Rani R, Thakur VK, Gupta M. New Insights in Topical Drug Delivery for Skin Disorders: From a Nanotechnological Perspective. ACS Omega. 2023 Jun 6;8(22):19145–19167.
3. Brito S, Baek M, Bin B H. Skin Structure, Physiology, and Pathology in Topical and Transdermal Drug Delivery. Pharmaceutics. 2024 Oct 31;16(11):1403.
4. Bhuyan C, Saha D, Rabha B. IJ Pharm Res Int. 2021 Oct 26;33(47A):344–357.
5. Kolarsick PAJ, Kolarsick MA, Goodwin C. Anatomy and physiology of the skin. In: James WD, Berger TG, Elston DM, editors. Andrews' Diseases of the Skin: Clinical Dermatology. 10th ed. Philadelphia: Elsevier Saunders; 2006. p. 1–14.
6. Lotfollahi Z. The anatomy, physiology and function of all skin layers and the impact of ageing on the skin. Wound Practice and Research. 2024; 32(1):6–10.
7. P.B. Patil, S.K. Datir, R.B. Saudagar. A Review on topical gels as drug delivery system, Journal Of Drug Delivery and Therapeutics. 2019; 9(3): 989-994.
8. Oliveira R, Almeida IF. Patient-Centric Design of Topical Dermatological Medicines. Pharmaceuticals (Basel). 2023; 16(4): 617.

9. Kelly BP. Superficial fungal infections. Pediatrics in Review. 2012 Apr; 33(4): e22–e37.
10. Grappel SF, Bishop CT, Blank F. Immunology of dermatophytes and dermatophytosis. Bacteriological Reviews. 1974 Jun; 38(2): 222–250.
11. Keshwania P, Kaur N, Chauhan J, Sharma G, Afzal O, et al. Superficial Dermatophytosis across the World's Populations: Potential Benefits from Nanocarrier-Based Therapies and Rising Challenges. ACS Omega. 2023 Aug 22; 8(35):31575–31599.
12. Fidel PL Jr, Wozniak KL. Superficial Candidiasis. In: Topley & Wilson's Microbiology and Microbial Infections. Chichester, UK: John Wiley & Sons, Ltd; 2010.
13. Djearamane S, Xiu L-J, Wong L-S, Rajamani R, Bharathi D, et al. Antifungal Properties of Zinc Oxide Nanoparticles on Candida albicans. Coatings. 2022;12(12):1864.
14. Renati S, Cukras A, Bigby M. Pityriasis versicolor. BMJ. 2015 Apr 7;350:h1394.
15. Hassan MN, Hussain M, Sana A, Muzammal F, Saeed Z, et al. Nanoparticles Arsenal, Emerging Innovations as Antifungal Agents Against Candidiasis. Journal of Xi'an Shiyou University, Natural Science Edition. 2024; 20(6):42–58. ISSN: 1673-064X.
16. Rathore R, Gupta RD. Topical gel: a review. Int J Pharm Res Rev. 2013;2(8):18-27.
17. Yudaev P, Mezhuev Y, Chistyakov E. Nanoparticle-Containing Wound Dressing: Antimicrobial and Healing Effects. Gels. 2022;8(6):329.
18. Sheikh-Oleslami S, Tao B, D'Souza J, Butt F, Suntharalingam H, Rempel L, Amiri N. A Review of Metal Nanoparticles Embedded in Hydrogel Scaffolds for Wound Healing In Vivo. Gels. 2023;9(7):591.
19. Koukaras EN, Papadimitriou SA, Bikiaris DN, Froudakis GE. Insight on the formation of chitosan nanoparticles through ionotropic gelation with tripolyphosphate. Mol Pharm. 2012 Oct 1;9(10):2856–62.
20. Nava-Arzaluz MG, Piñón-Segundo E, Ganem-Rondero A, Lechuga-Ballesteros D. Single emulsion-solvent evaporation technique and modifications for the preparation of pharmaceutical polymeric nanoparticles. Recent Pat Drug Deliv Formul. 2012 Dec;6(3):209–23.
21. Quintanar-Guerrero D, Allémann E, Fessi H, Doelker E. Preparation techniques and mechanisms of formation of biodegradable nanoparticles from preformed polymers. Drug Dev Ind Pharm. 1998.
22. Date AA, Patravale VB. Microemulsions: applications in transdermal and dermal delivery. Crit Rev Ther Drug Carrier Syst. 2007;24(6):547–96.
23. Fessi H, Puisieux F, Devissaguet JP, Ammoury N, Benita S. Nanocapsule formation by interfacial polymer deposition following solvent displacement. Int J Pharm. 1989 Oct 1;55(1):R1–R4.
24. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. J Control Release. 2001 Jan 29;70(1-2):1–20.
25. Kanawade D, Gavdekar N. Review: Topical drug delivery system. International Journal of Pharmaceutical Research and Applications. 2021;2249-1781.
26. Prachi B. Shekhawat. Preparation and evaluation of Clotrimazole nanostructured lipid carrier for topical delivery, International Journal of Pharma and Bio sciences. 2013;4(1):407-416.
27. Samadhan K Deore, Rajendra K Surawase, Avish Maru. Formulation and evaluation of nanoemulsion of ketoconazole, Research

Journal of Pharmaceutical Dosage Forms and Technology. 2019;11(4):269-264.
28. Jadhav K, Jadhav S, Sonawane D, Somvanshi D, Shah H, Patil P. Formulation and evaluation of miconazole nitrate loaded novel nanoparticle gel for topical delivery. J Pharm Res Int. 2021;33(44A):292-307.
29. Jyoti Saxena, Pranshu Tangri, Vikas Jakhmola, N.G. Raghvendra Rao. Preformulation studies on a drug: Miconazole, International Research Journal of Engineering and Technology. 2020; 7(2): 729-736.
30. Bader Mubarak Aljaeid, Khaled Mohamed Hosny. Miconazole-loaded solid lipid nanoparticle: formulation and evaluation of a novel formula with high bioavailability and antifungal activity, International Journal of Nanomedicine. 2016; 441-447.
31. Reddy KS, Azam Khan K.K., Nagaraja. C. A Review on the determination of melting point measurement system, International Journal of Advanced Research in Electrical, Electronics and Instrumentation Engineering. 2016; 5(2): 338-946.
32. Nina Alizadeh, Reza Ansari, Nasibehrezace. Extractive spectrophotometric determination of miconazole, Journal of Pharmaceutical and Health Science. 2012; 1(4): 45-52.
33. Sajal Jain, Sanjay Jain, Piush Khare, Aravind Golbalka, Divya Bansal, Sanjay. K Jain. Design and development of solid lipid nano particles for topical delivery of anti-fungal. 2010; 17(6): 443-451.
34. Isac, G. Deagvero, Hal Nural Huda, Victor Rodriguez, Jade Zicasi, Taslim A., Al-Hial, Abu Zyed Hal Badruvdoza, Mel Nuronnabi. Nano-Vesicle Based Antifungal Formulation Shows higher stability skin diffusion bio safety and antifungal efficacy in-vitro. 2020; 1-12.
35. Amit Kumar Singh, HOK Mukerjee, Himanshu Ramdey Shanti Bhushan Mishra. "Fabrication of solid lipid nanoparticles by hot shear homogenizer and optimization by box Behnken design: an accelerated stability assessment, Journal of Applied Pharmaceutical Science. 2021; 11(09): 035-047.
36. Mariyam S, Roy N, Sharma R, Gupta S, Khan H, Agarwal S. Design and Evaluation of Miconazole Nitrate loaded Nanostructured Lipid Carriers (NLC) for improving the Antifungal therapy. J Appl Pharm Sci. 2013 Jan;3(1):46-54.
37. Anju K P, Shripathy D, Shabaraya A R. Antifungal topical nanoemulgel containing miconazole nitrate, International Journal of Health Sciences and Research.2021;11(11):208-229.
38. Pedrosa SS, Gonçalves C, David L, Gama M. A novel crosslinked hyaluronic acid nanogel for drug delivery. Macromol Biosci. 2014 Nov;14(11):1556-68.
39. Ain S, Ain Q, Chauhan S, Yadav M, Singh SV, Kumari B. Preparation and evaluation of ketoconazole nanogel for topical application. Eur Chem Bull. 2025;14(1):61-75.
40. Kandge M, Chougule M, Bhinge S. Formulation and evaluation of microemulsion containing miconazole nitrate. Asian Journal of Pharmaceutical Research and Development. 2019;7(3):15-20.
41. Pavia DL, Lampman GM, Kriz GS, Vyvyan JR. Introduction to Spectroscopy. 5th ed. Stamford: Cengage Learning; 2015. p. 26-30.
42. Beckett AH, Stenlake JB. Practical Pharmaceutical Chemistry. 4th ed. New Delhi: CBS Publishers and Distributors; 2002. p. 275-300.
43. Koshti D, Mishra R. Formulation and evaluation of nanogel containing Aloe barbadensis. Int J Pharm Biol Arch. 2020;11(1):35-41.

44. Pokhriyal A, Tripathi G. Evaluation parameters of nanoparticles: A review. Der Pharmacia Lettre. 2022;14(3):24-29.
45. Chawalke P, Zafar A, Binshaya AS, Al Shmrany H, Hazazi A, Abalkhail A, et al. Topical miconazole nanogel: in vitro characterization, in vivo skin irritation, and enhanced antifungal efficacy. Drug Dev Res. 2025;86(4):e70106.
46. Sanap GS, Mohanta GP. Design and evaluation of miconazole nitrate loaded nanostructured lipid carriers (NLC) for improving the antifungal therapy. J Appl Pharm Sci. 2013;3(1):46–54..

HOW TO CITE: Jagadish G., Prajwal R.*, Manasa P., Manoj M., Anju K. P., Formulation and Evaluation of Miconazole Nitrate Loaded Nanoparticle Gel, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 11, 2239-2277 https://doi.org/10.5281/zenodo.17615314