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Formulation and evaluation of microemulsion containing miconazole nitrate

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***Abstract*---**The aim of the present research is to formulate a microemulsion containing miconazole nitrate as it provides various advantages over conventional dosage form. It also put forward the idea for the formulation of microemulsion containing miconazole nitrate with the use of varying surfactant and co- surfactants with an objective to increase the better drug loading, high transparency, high thermodynamic stability, better bioavailability and ease of preparation. Miconazole nitrate is hydrophobic imidazole antifungal agent. The studies show that it is highly effective in the topical treatment of fungal infections. Due to the presence of both lipophilic and hydrophilic domains, a wide range of lipophilic and hydrophilic domains are incorporated in these systems.

***Keywords*---**formulation, microemulsion, miconazole nitrate.

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Introduction

Skin diseases can be generally treated by topical or delivering directly drug into dermis. These are normally applicable to superficial infections, also which are restrained to stratum corneum. A wide range of technologies have been developed to overcome these problems such as liposomes, chemical penetration, microemulsion, sonophoresis, iontophoresis, electroporation, and stratum corneum abscission. Miconazole nitrate is an imidazole antifungal agent which shows fungistatic activity in opposition to normal pathogenic fungi as well as yeasts. Depending upon the structure, microemulsions are of different types as w/o, o/w or bicontinuous system. Microemulsion is defined as clear, stable and isotropic mixtures of oil, water, surfactant and co- surfactant. This drug delivery is used for topical, percutaneous, transdermal, oral, parenteral and ocular application of medicinal agents. All microemulsion are fluids with low viscosity. The miconazole nitrate is primarily known for its antifungal activity. It is clinically used for superficial treatment of superficial mycoses, dermatophytes, cutaneous candiasis and other infections. Topical drug therapy is appropriate for management of local diseases in order to restrict therapeutic effect to target size and decrease systemic drug absorption. Miconazole Nitrate is generally applied topically for treating various diseases on skin surface like athlete's foot, jock itch, ringworm and perioral candidiasis.

Materials and Methods

Miconazole nitrate was purchased from Solanki Suppliers (Pune, India). Oleic acid and Tween 20 were purchased from Solanki Suppliers (Pune, India). Chemicals such as propylene glycol was obtained from the laboratory. All the chemicals obtained were of analytical grade.

Methods

Identification of pure drug

Identification of pure drug was carried by Fourier Transform Infra-red spectrophotometry (Shimadzu 800s) scanned in the range of 200-400 nm.

FTIR Study

FTIR (Shimadzu 8400s) spectrophotometer was used in the range of 400-400 cm^{-1} using potassium bromide discs (mixing ratio 1:1). The samples were properly sealed in aluminium pans and heated at a constant rate of 10 ℃/min over a temperature range of 40-300 ℃.

Determination of Melting point

Melting point of drug was determined by Thiele's tube method. The small amount of drug was taken in one end closed capillary tube is attached to graduated thermometer and constant heat was supplied to the assembly suspended in paraffin bath. The temperature at which the drug melts is noted.

Preparation of Microemulsion

The required amount of miconazole nitrate was weighed. The weighed amount of drug was dissolved in oil phase (mixture 1). This mixture was sonicated for 10 min. The mixture 2 is prepared by mixing surfactant and co- surfactant. The prepared mixture was mixed together using magnetic stirrer. The drop wise addition of water was done for making up the volume. The 100 ml microemulsion was prepared.

Table 1
Preparation of Microemulsion (Batch 1- Batch 4)

Ingredients	Batch 1	Batch2	Batch 3	Batch 4
Griseofulvin (gm)	1	1	1	1
Oleic acid (ml)	7	7	7	7
Tween 20(ml)	30	25	20	15
Propylene glycol (ml)	30	28	26	24
Distilled water(ml)	32	39	46	53

Evaluation of microemulsion
pH

The pH of prepared microemulsion was measured using digital pH meter. It is measurement of alkanity or acidity for the prepared microemulsion

Viscosity

Viscosity was determined using (LV) Brookfield Viscometer using. Spindle no. 62. Microemulsion shows Newtonian type of flow. Viscosity was measured for fixed time 2 min

Zeta potential

Zeta potential is used to determine the stability of the prepared microemulsion. The charge on the surface of the particles was characterized by HORIBA SZ-100 by measuring the Zeta potential of the microemulsions. The sample was injected into a disposable cell and measurement of the particle electrophoretic moiety results in the calculation of Identification potential.

Particle size

Samples were diluted using distilled water followed by measurement of particle size and Zeta potential in the triplicates and average values. Particle size of microemulsions was determined using HORIBA sz-100 (z type).

Conductivity

The Conductivity of prepared microemulsion was measured by digital conductivity meter. Voltage was applied between two electrodes in a probe immersed in a sample. The drop in voltage caused by resistance of sample was used to calculate the conductivity per centimetre

Scanning Electron Microscopy

Scanning electron microscopy provides high resolution imaging that may be used to evaluate diverse materials for surface cracks, defects contaminants and corrosion. When a focused stream of secondary electron interacts with atoms in sample, multiple singles produced that include information about the surface topography using Nova NanoSEM NPEP. All the images are canned at 10000 x with a 5 m dimension scale 303.

Content Uniformity

Drug content was performed by dissolving accurately weighed 1 ml of microemulsion in methanol. After suitable dilution absorbance was recorded by using UV visible spectrophotometer (UV 1800, Shimadzu, Japan) at 232 nm. Drug content was measured by slope of standard curve.

Results

FTIR Study

Identification and confirmation of drug was carried out by observing the spectra.

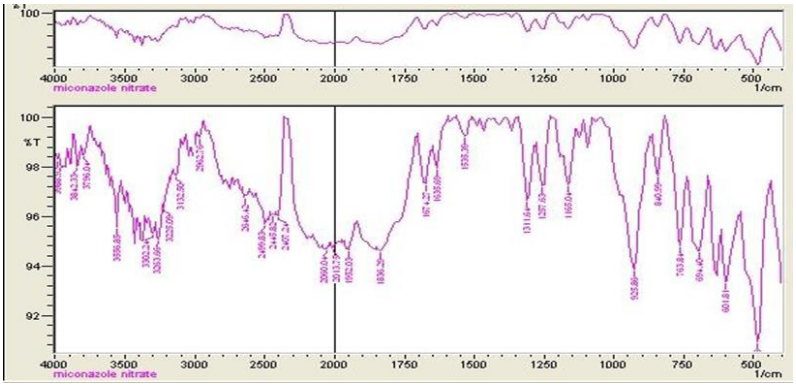

Fig 1. Interpretation of IR of Miconazole Nitrate

Identification of pure drug shows C - C stretching vibrations at 1505 cm^{-1}, C- H bending at 1468 cm^{-1}, the C-N vibration of imidazole group at 3151 cm^{-1}

UV Spectroscopy

The calibration curve was obtained by plotting the absorbance versus the concentration data was treated by linear regression analysis. The equation of

linearity curve for miconazole nitrate was obtained by the equation y= 0.0275x + 0.0335. The linearity curve was found to be linear for the above-mentioned concentrations. The correlation coefficient R of drug was found to be 0.9965.

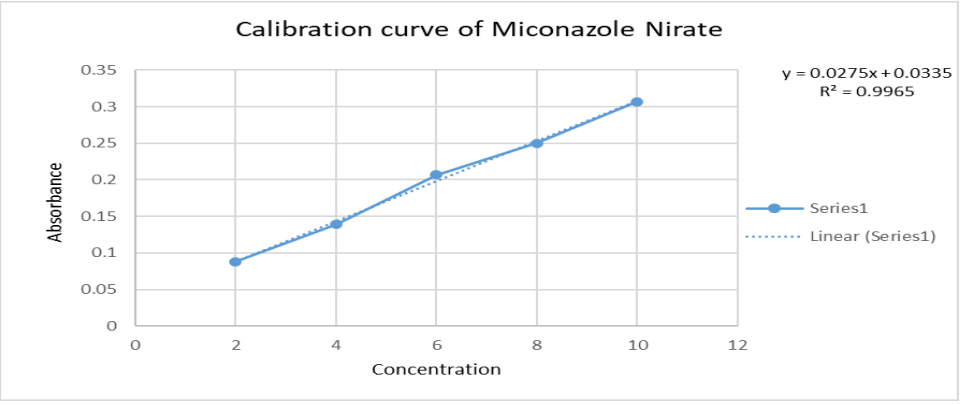

Fig 2. Calibration curve of Miconazole Nitrate

Melting point

The melting point of Miconazole nitrate was found to be 180℃.

pH, Drug content

Table 2
Characterisation of microemulsion

Batch	pH	Drug content (%)
1	6.2	96.89
2	6.5	92.54
3	5.8	94.23
4	6.1	90.65

The pH of microemulsion should be always considered within the suitable range. The pH of different microemulsion was checked as followed in the table. Drug content is determined as shown in the table. The higher amount of drug will show concentrated formulation. These formulation ranges from concentrated to aqueous.

Particle Size and zeta potential

Table 3
Determination of Particle size and Zeta potential

Batch	Particle Size(nm)	Zeta Potential(mV)
1	215.0	-20.5
2	226.9	-18.9
3	802.7	-17.9
4	172.4	23.6

The particle size of microemulsion determines the rate and extent of drug release absorption. The small particle size of microemulsion show more rapid absorption as well as it increases the bioavailability of the formulation. Particle size of optimized microemulsion (M1) was found to be 215.0 nm these globules are suitable for topical delivery administration. The Zeta potential plays a crucial role in the stability factor of the formulation. The high value of Zeta potential indicates the electrostatic repulsion between the two droplets. The negative charge characterizes the more stability of the formulation. The Zeta potential value for optimized batch M1 was determined to be -20.5. It shows better stability.

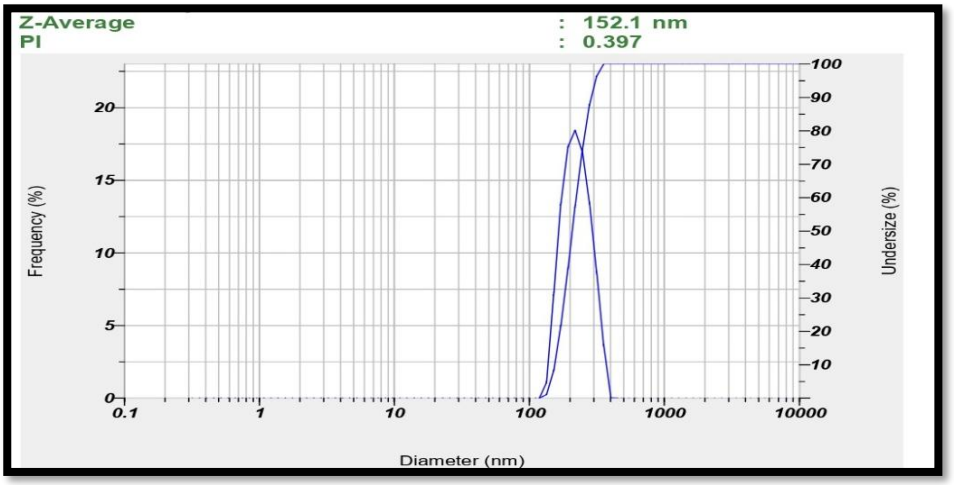

Fig 3. Particle size of optimized formulation (M1)

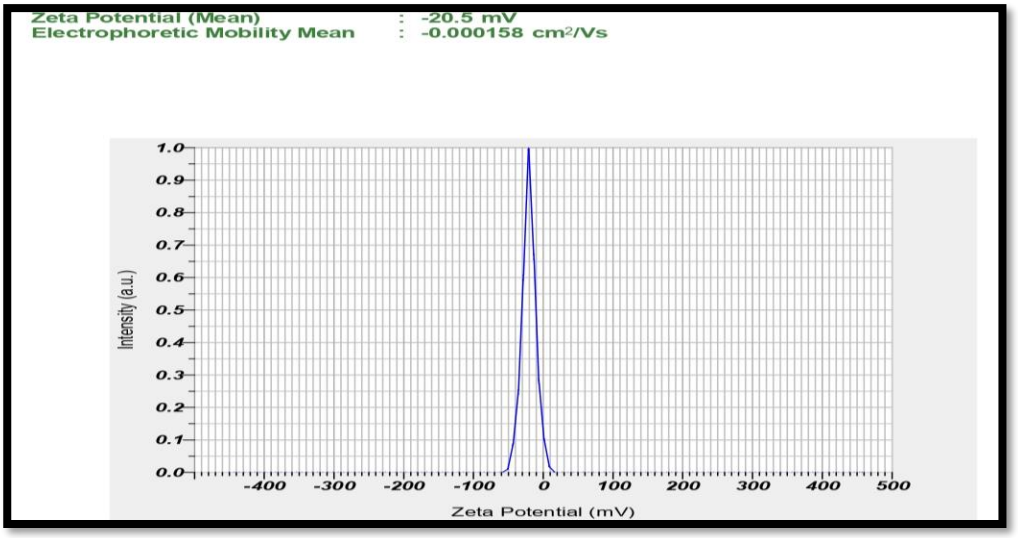

Fig 4. Zeta potential of optimized formulation (M1)

Viscosity

The viscosity values for different formulation are considered in the table:

Table 4
Viscosities of microemulsion

RPM	Batch 1	Batch 2	Batch 3	Batch 4
10	144	193	264	1428
20	165	155	185	936
30	168	149	149	737
50	171	151	110	553.2
100	172.3	152	84.30	551

Conductivity

Table 5
Determination of electrical conductivity

Batches	200ms	20ms	2 ms	200 µs	20 µs
1	000	00.0	0.02	023	1.
2	000	00.0	0.04	036	1.
3	0.0	00.0	0.03	031	1.
4	000	00.0	0.01	014	1.

Electrical conductivity is used to determine the nature of w/o or o/w microemulsion. It is measured using electric conductometer. It is used to identify whether there is oil or water as a continuous phase. It is also used to identify the phase inversion process.

Scanning Electron Microscopy

The optimized batch of. Microemulsion which is analysed for SEM Analysis shows the hexagonal or bicontinuous structure. It is also further analysed for surface topography and morphology of the sample.

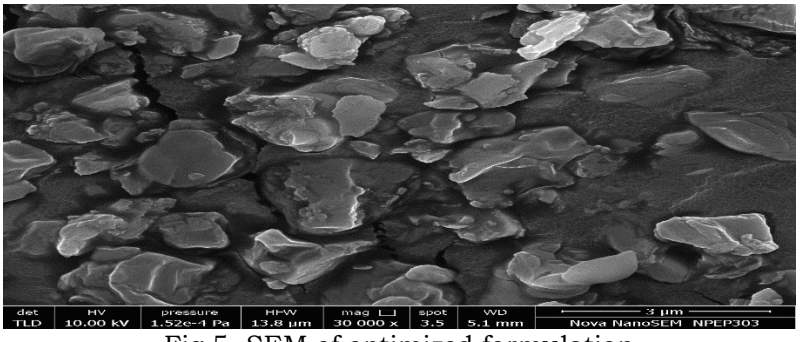

Fig 5. SEM of optimized formulation

Conclusion

Different administration of drug is considered as the basic criteria for the choice of drug as well as its route. Microemulsion shows thermodynamic stability, choice of route for control delivery. The above formulation shows good consistency. Miconazole nitrate is considered from the azole group of antifungals. They prove to be best formulation in the novel drug delivery system since they have prolonged shelf life, improved drug solubilization and ease of preparation and administration. The idea behind the study was to develop a topical microemulsion for sparingly soluble antifungal agent. Another advantage for formulation of microemulsion is most of the lipophilic groups are easy to penetrate through the microemulsion as compared to other drug delivery. The above optimized microemulsion shows all the parameters within the suitable criteria. The Zeta potential characterizes the stability of the optimized microemulsion. These is considered as important factor for the optimized batch.

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