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# Formulation and Evaluation of Solid Lipid Nanoparticles of Bifonazole

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## ABSTRACT

The objective of this study was to develop suitable solid lipid nanoparticles for topical delivery of Bifonazole. Bifonazole is an imidazole antifungal drug used in form of ointments. It was patented in 1974 and approved for medical use in 1983. Bifonazole having broad spectrum activity against dermatophytes, moulds, yeasts, fungi and some gram positive bacteria. BFZ SLNs systems were developed by melt emulsification followed by solvent evaporation technique using Compritol 888ATO (Glyceryl behenate) as a solid lipid and Tween 80 as a surfactant. Developed SLNs were evaluated for particle size, polydispersity index (PI), entrapment efficiency (EE) and drug release profiles. Process and formulation parameters were optimized. Differential scanning calorimetry (DSC) and X-ray diffraction (XRD) studies were carried out on SLNs to mark the changes in the drug and lipid modifications. The BFZ SLNs based gels were prepared using Carbopol 940 as a gelling agent. The SLNs based gels were evaluated for rheological parameters, in vitro drug release and permeation studies. In vitro antifungal study suggested that the SLNs based gel was more effective in inhibiting growth of Candida albicans. Thus the study concludes that SLNs based gel of BFZ gives a sustained release profile of BFZ and has the potential for treatment of topical fungal infections.

Keywords: Comprisal 888ATO, XRD

## I. INTRODUCTION

Solid lipid nanoparticles (SLNs) are colloidal carrier systems developed in the beginning of 1990s as alternative to existing pool of carrier systems such as particles, liposomes and polymeric nanoparticles for the delivery of poorly water soluble drugs. SLNs combine their advantages such as controlled release, biodegradability, and protection of active compounds[1-3]. SLNs have been used in topical delivery as they can allow penetration of drug into the skin, offer sustained release of drug to avoid systemic absorption. The system also reduces irritation to the skin as they are made up of biocompatible excipients most of them have been in an approved status or are excipients used in commercially available cosmetic or pharmaceutical preparations[1,2]

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Bifonazole (BFZ), 1-[phenyl(4-phenylphenyl) methyl]-1H-imidazole, is a substituted imidazole antifungal agent having a broad spectrum of activity against dermatophytes, moulds, yeasts, dimorphic fungi and some Gram-positive bacteria. BFZ is indicated in the treatment of superficial fungal infections of the skin such as dermatophytes, cutaneous candidiasis and pityriasisversicolor. It is practically insoluble in water with a very short halflife of 1-2 h and is minimally absorbed (0.6% of applied dose) following dermal application [3,4,5]

Since hyphae of fungi (mycelium) can penetrate deep into the epidermal layers by sliding past the corneocytes of the horny layer, improved penetration of the active ingredient is desired in antifungal therapy of the dermis [9]. Thus, topical application of SLNs based gel with increased penetration and retention through skin because of lipid nanoparticles will be much favorable for the treatment of infections and symptomatic relief. Hence, aim of present work was to formulate SLNs based gel of BFZ for topical application ultimately improving the efficacy of the drug

## II. METHODS AND MATERIAL

### Materials:

**Table 1.** Chemicals

| Sr.No. | Name of Chemical | Supplier / Manufacturer |
|---|---|---|
| 1. | Bifonazole | Medley Pharmaceutical, Mumbai |
| 2. | Compritol 888 ATO | Mohini organics, Mumbai |
| 3. | Poloxamer 188 | Mohini organics, Mumbai |
| 4. | Ethanol | Loba Chemie, Mumbai |
| 5. | Tween 80 | Loba Chemie, Mumbai |

### Methods:

#### 1) Preparation of SLNs:[6,7]

SLNs prepared by solvent evaporation method. The lipophilic material is dissolved in a water-immiscible organic solvent that is emulsified in an aqueous phase. Upon evaporation of the solvent, nanoparticles dispersion is formed by precipitation of the lipid in the aqueous medium by giving the nanoparticles of 25 nm mean size. The solution was emulsified in an aqueous phase by high pressure homogenization. The organic solvent was removed from the particle by evaporation under reduced pressure

### COMPOSITION OF BFZ SLN

**Table 2.** COMPOSITION OF BFZ SLN

| Batch Code | Bifonazole(%) | Compritol 888ATO(%) | Poloxamer 188(%) | Tween 80(%) |
|---|---|---|---|---|
| F1 | 1 | 2 | 2 | 1 |
| F2 | 1 | 3 | 2 | 1.5 |
| F3 | 1 | 3 | 1 | 2 |
| F4 | 1 | 2 | 1 | 1.5 |
| F5 | 1 | 2 | 3 | 1.5 |
| F6 | 1 | 4 | 1 | 1.5 |
| F7 | 1 | 3 | 3 | 2 |
| F8 | 1 | 4 | 3 | 1.5 |
| F9 | 1 | 2 | 2 | 2 |
| F10 | 1 | 4 | 2 | 2 |
| F11 | 1 | 3 | 3 | 1 |
| F12 | 1 | 4 | 2 | 1 |
| F13 | 1 | 3 | 1 | 1 |

#### 1.1) Evaluation and characterization of BFZ SLNs:[8,9,10]

nanoparticles were evaluated for following parameters:

**1.Drug content:**

nanoparticle equivalent to 10 mg of Bifonazole was taken in 10 ml volumetric flask containing 5 ml ethanol and stirred for 30 min. Volume was made up to 10 ml with ethanol. From the above solution, 1 ml was further diluted with 10 ml ethanol to get 100µg/ml. The resultant solution was filtered through Whatman filter paper and absorbance of the solution was measured at 255 nm using UV spectrophotometer.[18]

**2.Appearance:**

The prepared nanoparticles were inspected visually for clarity, color and presence of particles

**3.Particle size:** Particle size and size distribution measurement of Nanoparticle was carried out by dynamic light scattering using Malvern Hydro 2000 SM particle size analyzer (Malvern instruments, UK). Nanoparticle was added to the sample dispersion unit with stirrer, and stirred so as to minimize the particulate aggregation by inter particle interaction. For the measurement the laser obstruction range was maintained between 25%. The analysis was performed thrice and average hydrodynamic particle size was expressed as the value of z-average size ± SD.

**4) Solubility of drug in optimized nanoparticle :**

2 g nanoparticle were taken, excess amount of drug was added into it. This composition was mixed for 72 hrs. on mechanical shaker. Centrifuge it, separate the supernatant layer make dilutions with ethanol and take readings. Following graph shows amount of drug soluble in mg/ml when they combined with each other.

**5) Stability study of nanoparticle :**

Stability testing evaluates a products ability to maintain its original aesthetic, physical and chemical characteristics under controlled conditions designed to accelerate aging. Such testing can provide an early indication of the problems that may occur in the formulations. The stability studies were carried out for the selected formulations which were placed in lacquered collapsible aluminum tubes. These tubes were subjected to room temperature for 2 months and then the transparency/ clarity, color change, viscosity and appearance was determined.

**2) Preparation of SLNs based gel:** [11,12]

The SLNs dispersion was converted into gel carrier system using gelling agents Carbopol . Gelling agent at various concentrations were dispersed under stirring in to the SLNs dispersion till they were uniformly mixed to form gel with suitable consistency The conventional gel was prepared by simply dispersing the drug into the gel matrix.

**2.1) Evaluation of nanoparticle based gel :**[13,14,15]

The Nanoparticle based topical gel formulations were evaluated for following parameters

**1) Drug content:**

For the determination of drug content 10 mg of nanoparticle based hydrogel was withdrawn from container and dissolved in sufficient quantity of ethanol and volume was made up to 10 ml and then specific dilutions were made with phosphate buffer pH 7.4. Then the absorbance was taken by UV spectrophotometer (UV visible spectrophotometer shimadzu) against blank with λmax 291nm and the drug content was calculated using standard graph.

**2) pH:**

All gels were analyzed with the pH meter to get the exact pH values. The pH of the hydrogel was

determined using digital pH meter, standardized using pH 4.0 and 7.0 standard buffers before use.[16,17,20]

**3) Rheology:**

The rheology of gels were determined using Brookfield rheometer R/S plus. The study contains the polymeric structure elasticity using creep and module as a functional unit, and also the viscosity behavior of hydrogel under different a) stress b) strains c) torque d) speed all conditions used for study were maintained throughout the experiment. The semisolid preparations should flow or deform after applying the force and regain its elasticity as the force is removed. Thus, to understand the rheological properties of gels and for selection of optimum concentration of polymer having desired rheological properties, different polymers were used to prepare nanoparticle based gels at room temperature. The rheology of all samples was required to determine and identifies the minimum concentration of polymer required for the formation of nanoparticle based gel with good viscoelasticity properties. These properties were indirectly correlated to the gel characteristics such as consistency, appearance, Spreadability and dispersibility.[22,23]

**4) In vitro drug release and their kinetics:** In vitro drug release study was determined for different batches of gel using Franz diffusion cell with artificial membrane.[19,20,]

**5) Spreadability:** Spreadability is an important property of topical and transdermal formulations from patient compliance point of view. Applications of the formulation on inflamed part would be more comfortable if the base spreads easily exhibits maximum 'slip' and 'drag'. The spreadability of the nanoparticle based gel formulations was determined by a weighed quantity of gel was taken on glass plate (8cm). Another glass plate (8cm) was dropped from a distance of 5 cm. The diameter of the circle of spread was measured after1 min. Types of gels based on spreadability are given in table.[23]

**6) Antifungal activity study using cup plate method**

The cup plate agar diffusion method was employed to assess the antifungal activity of the prepared gels. 20 ml of the inoculated nutrient agar were distributed into sterile petri dishesh. The agar was left to set and in each of these plates, 5 mm in diameter, were cut using a sterile cork borer No. 4 and the agar discs were removed. Alternate cups were fitted with 20µl of each formulation using microliter pipette and allowed to diffuse at room temperature for two hrs. The plates were then incubated in the upright position at $37^0$C for 18 hrs. The respective solvents were used as controls. The diameters of the growth inhibition zones were measured at 24, 48 and 72 hrs of incubation averaged and the mean value were tabulated.

1) 7. Stability:[13]

The optimized formulation nanoparticle based gel NBG2were evaluated for stability after preparation for time span 30 days, 45 days and 60 days at $30^0$C. The following parameters were evaluated

1) pH
2) Color
3) % drug content

It is observed that formulation do not give significant changes after preparation. The viscosity of gel was in acceptable limit after day 60.

## III. RESULTS AND DISCUSSION

### A) Evaluation of solid lipid nanoparticle

**1) Drug content**: Nanoparticle equivalent to 10 mg of Bifonazole was taken in 10 ml of ethanol (conc. becomes 1 mg/ml). From above solution 0.1 ml was taken and further diluted with 10 ml of ethanol (conc. becomes 10µg/ml) absorbance was measured under λmax 255nm. Using UV spectrophotometer against blank and the drug content was calculated using standard graph. Standard equation i.e.

Y= MX+ C

Where,

Y is absorbance,
X is concentration,
C is intercept on Y axis,
R2 is regression coefficient.
Y=0.0621x

$R^2 = 0.9918$

**Table no.**3 % Drug content of formulated batches.

| Sr. No. | Batch No. | % Drug content |
|---|---|---|
| 1 | F1 | 56.97 |
| 2 | F2 | 60.69 |
| 3 | F3 | 53.48 |
| 4 | F4 | 63.95 |
| 5 | F5 | 61.16 |
| 6 | F6 | 72.79 |
| 7 | F7 | 78.83 |
| 8 | F8 | 80.51 |
| 9 | F9 | 82.56 |
| 10 | F10 | 85.59 |
| 11 | F11 | 85.96 |
| 12 | F12 | 86.64 |
| 13 | F13 | 87.92 |

Calculation for getting concentration

Y=0.0621x

X=…… µg/ml

% Drug content

Theoretical drug content=10 µg/ml is 100%

So,% drug content = calculated value of concentration / theoretical value

The drug content of most batches lies above 60 % which complies with IP limit.

**2) Appearance:**

The prepared nanoparticle gels were inspected visually for clarity, colour and presence of any particle.

**Table no.4** Appearance of Formulated Nanoparticle Batches.

| Batch Code | colour | Clearity |
|---|---|---|
| F1 | Pale yellow | Clear |
| F2 | Pale yellow | Clear |
| F3 | Pale yellow | Clear |
| F4 | Pale yellow | Clear |
| F5 | Pale yellow | Clear |
| F6 | Pale yellow | Clear |

Mean±SD ; n=3

The appearance of almost all batches is clear which indicates the nanoparticles are stable

**3) Particle size**

Particle size and size distribution measurement of Nanoparticle was carried out by dynamic light scattering using Malvern Hydro 2000 SM particle size analyzer (Malvern instruments, UK). nanoparticle was added to the sample dispersion unit with stirrer, and stirred so as to minimize the particulate aggregation by interparticle interaction. For the measurement the lazer obscuration range was maintained between 25%. The analysis was performed thrice and average hydrodynamic particle size was expressed as the value of z-average size.

**Table no.5** Particle size of Formulated Nanoparticle Batches.

| Sr. no. | Batch no. | Avg. particle size(nm) |
|---|---|---|
| 1 | F1 | 205.6 |
| 2 | F2 | 350.2 |
| 3 | F3 | 324.1 |
| 4 | F4 | 165.4 |
| 5 | F5 | 235.6 |

| | | |
|---|---|---|
| 6 | F6 | 237.6 |
| 7 | F7 | 120.4 |
| 8 | F8 | 150.6 |
| 9 | F9 | 260.6 |
| 10 | F10 | 354.1 |
| 11 | F11 | 183.1 |
| 12 | F12 | 213.5 |
| 13 | **F13** | **54.8** |

**4) Solubility of drug in optimized nanoparticle :**

The drug was more soluble in nanoparticle as compare to individual nanoparticle components.

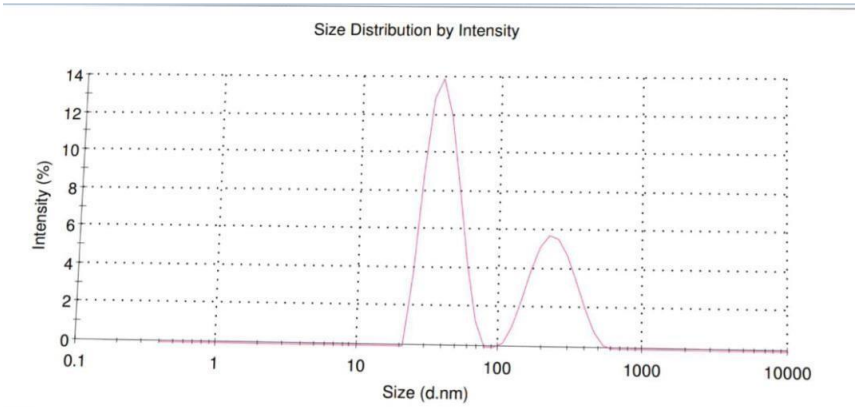


**Fig. no.1** Particle size graphical distribution F13 Optimized Nanoparticle

**Table no.6** Solubility of Bifonazole in nanoparticle

| **Batch No.** | **Solubility mg/ml** |
|---|---|
| **F13** | **18.53** |

**5) Stability studies :**

The chemical and physical stability of Bifonazole nanoparticle was studied via clarity, phase separation observation and drug content for up to 2 months.

**Table no.7** Stability study of nanoparticle F13

| **Visual observation** | **Stability condition** | **0th day** | **30th day** | **60th day** |
|---|---|---|---|---|
| clarity | Room Temp | Very Good | Good | Good |
| Color change | Room Temp | No color change | No color change | No color change |

**B) Selection of Polymer for gel:**

Bioadhesive polymers are selected for preparation of topical gel.

The polymer which gives sufficient viscosity and stability are selected for further study. Following polymers were studied for viscosity of 3 % concentration at 30 rpm.

**Table no.8** Selection of polymer for gel

| **Sr. no.** | **Polymers** | **Viscosity (Pa.S)** |
|---|---|---|
| 1 | HPMC K 100 | 32.25±0.42 |
| 2 | HPMC K 7 | 24.23±0.23 |
| 3 | Carbopol 971 G | 26.24±0.5 |
| **4** | **Carbopol 934** | **38.26±0.58** |

From above data carbopol 934 and carbopol 940 were given sufficient viscosity and stability. Carbopol 934 produces clear and transparent gel than carbopol 940. For the preparation of gel Carbopol 934 selected as mucoadhesive polymer.

**C) Preparation of nanoparticle based gel:**

The optimized formulation of nanoparticle was taken for preparation of gel.

**Table no.9.** Viscosity and drug release of different polymeric gels

| **Sr. no.** | **Name of polymer** | **Conc. of polymer** | **Viscosity in Pa.S.** | **% Drug release at 8 hr.** |
|---|---|---|---|---|
| 1 | Carbopol 934 | 0.5% | 27.36 | 95.71±0.87 |
| 2 | | 1.0% | 33.35 | 81.68±0.21 |
| 3 | | 1.5% | 34.68 | 64.21±0.85 |
| 4 | | 2.0% | 36.58 | 62.25±0.35 |
| 5 | Pure drug | 1.0% | 28.23 | 81.15±0.25 |

The different concentration ranges from 0.5, 1.0, 1.5, 2.0 and 2.5 % were prepared and nanoparticle was mixed with gel base. Following batches were prepared and evaluated for various parameters.

**Table no.10.** composition of Nanoparticle based gel.

| Sr. no. | Conc. of polymer | Conc. of Nanoparticle batch F13 | Conc. of gel base | Batch code |
|---|---|---|---|---|
| 1 | 0.5% | 50% | Up to 100% | NBG1 |
| 2 | 1% | 33.33% | Up to 100% | NBG2 |

**D) Evaluation of nanoparticle based gel :**

The nanoparticle based gel was evaluated for the following parameters.

**i. Drug content:**

Nanoparticle based gel equivalent to 10 mg of Bifonazole was taken in 10 ml of ethanol (conc. becomes 1 mg/ml). From above solution 0.1 ml was taken and further diluted with 10 ml of ethanol (conc. becomes 10µg/ml) absorbance was measured at λmax 291nm. using UV spectrophotometer against blank and the drug content was calculated using standard graph. nanoparticle based gel batch F13 formulations having more drug content as compared to other and it matches with the standard limit of IP hence it was used for further study.

$Y= MX+ C$

Where,

Y is absorbance,

X is concentration,

C is intercept on Y axis,

R2 is regression coefficient.

$Y=0.0621x$

$R^2 = 0.9918$

**Table no.11**. % Drug content of formulated batches.

| Sr. No. | Batch No. | % Drug content |
|---|---|---|
| 1 | F1 | 56.97 |
| 2 | F2 | 60.69 |
| 3 | F3 | 53.48 |
| 4 | F4 | 63.95 |
| 5 | F5 | 61.16 |
| 6 | F6 | 72.79 |
| 7 | F7 | 78.83 |
| 8 | F8 | 80.51 |

| | | |
|---|---|---|
| 9 | F9 | 82.56 |
| 10 | F10 | 85.59 |
| 11 | F11 | 85.96 |

Y= MX+ C

Where,

Y is absorbance,

X is concentration,

C is intercept on Y axis,

R2 is regression coefficient.

Y=0.0621x

$R^2 = 0.9918$

**Table no.12.** % Drug content of formulated batches.

| Sr. No. | Batch No. | % Drug content |
|---|---|---|
| 1 | F1 | 56.97 |
| 2 | F2 | 60.69 |
| 3 | F3 | 53.48 |
| 4 | F4 | 63.95 |
| 5 | F5 | 61.16 |
| 6 | F6 | 72.79 |
| 7 | F7 | 78.83 |
| 8 | F8 | 80.51 |
| 9 | F9 | 82.56 |
| 10 | F10 | 85.59 |
| 11 | F11 | 85.96 |

**Time Vs % DR of Three batches.**

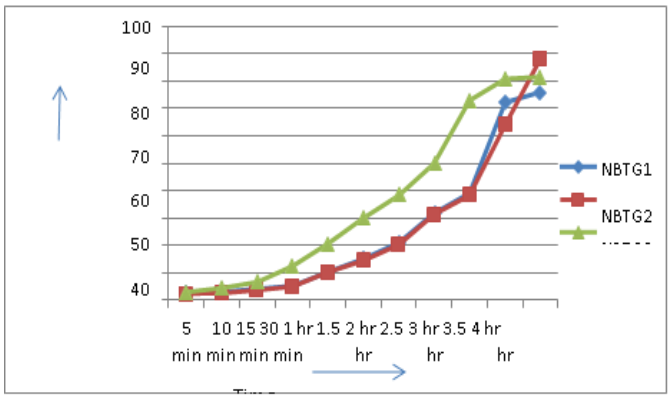


**Fig No.2** Time Vs % DR of Three batches

The nanoparticle based gel NBG2 formulation gives highest drug release but due to optimum viscosity of NBG2 is selected as optimized formulation. Various mathematical models were evaluated considering the dissolution profile of the Nanoparticle based gel formulations. In order to obtain the rate of release, the release data from the gel matrices were fitted to the following mathematical models: zero order kinetic, first order kinetic, square root of time equation (Higuchi equation and Peppas model).

**2) PH** The pH of nanoparticle based gel was determined using digital pH meter, standardized using pH 4.0 and 7.0 standard buffers before use. Then about 25 ml of Nanoparticle was taken in a small glass beaker and electrode was dipped into it for 1 min and pH was noted. From the following table it could be concluded that the prepared nanoparticle based gel formulation having pH nearer to skin pH and hence it is suitable for topical application.

The skin pH is 5 to 5.6 and observed pH range matches with the standard.

**Table no.** 13 pH of nanoparticle based gel

| Sr. no. | Batch no | pH |
|---|---|---|
| 1 | NBG1 | 6.4 |
| **2** | **NBG2** | **6.8** |

**3) Rheology:**

Apparatus: Brookfield rheometer R/S plus Spindle number: C- 75

Rpm: 50

**Table no 14** Rheological parameters of optimized NBG2

| Day | Viscosity (Centipoises) |
|---|---|
| Fresh | 867 .18 |
| First day | 892.01 |
| Second day | 907.26 |

**4) In vitro drug diffusion and their kinetics**

In vitro drug diffusion study were determined for different batches of gel using franz diffusion cell with artificial sigma dialysis `membrane the standard conditions was maintained throughout the experiment.

Conditions of experiment

1) Instrument name: Franz diffusion cell apparatus
2) Buffer solution: 6.8 Phosphate buffer solution
3) Name of membrane: Sigma dialysis membrane
4) Temperature: 37± $0.5^0$C
5) Stirring rpm: 50
6) Withdrawal: 2 ml

**Table no.** 15 Drug release study of nanoparticle based gel

| Sr. no | Batch no | % drug release |
|---|---|---|
| 1 | NBG 1 | 75.92 |
| **2** | **NBG2** | **88.14** |

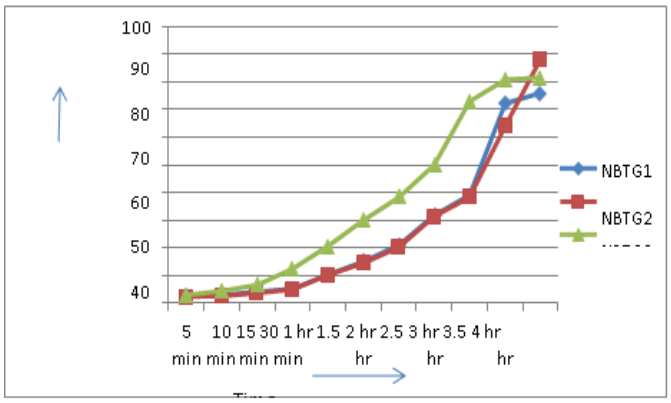


**Fig No 3** Time Vs % DR of Three batches

2) 5.Spreadability:

Spreadability of the Nanoparticle gel formulations was determined by a weighed quantity of gel taken on a glass plate (6.5cm). Another glass plate (6.5cm) was dropped from a distance of 5 cm. The diameter of a circle of

spread was measured after 1 min According to the table the Nanoparticle based gel NBG2 formulation having spreadability (3.93) and denotes the semifluid like gel. Nanoparticle based gel NBG2 (3.19) gives fluid like gel as the concentration of polymer increases the gel was thickened and spreadability was decreases. The optimized batch showing 3.93g.cm/s spreadability.

Formula - M×L/T

3) Table no.16. Spreadability study of nanoparticle based gel

| Sr. no | Batch no. | Conc. of polymer | Spreadability (gcm/sec) |
|---|---|---|---|
| 1 | NBG1 | 0.5% | 4.19 |
| 2 | NBG2 | 01.0% | 3.93 |

**6. Antifungal activity study using cup plate method**

**Table no.17.** Antifungal activity study using cup plate method

| Batches | Time span in hrs. | | |
|---|---|---|---|
| | 24 | 48 | 72 |
| Nanoparticle | 8.1mm | 12.4mm | 16.8mm |
| NBG2 | 11.5mm | 14.6mm | 21.3mm |

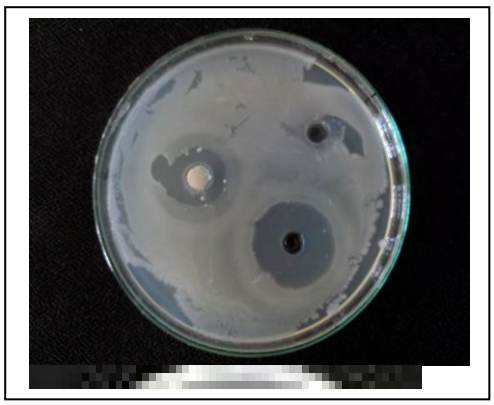

**Fig. no.4 A** Zone of inhibition for NBG2

**Figure no.4 B** Zone of inhibition for nanoparticle F13

The nanopaticle based gel NBG2 gives highest zone of inhibition as compare to F13 nanoparticle it could be concluded that the nanoparticle based gel formulation gives slow release of drug and after 72 hr the zone of inhibition was more than that of nanoparticle.

4) 7. Stability:

preparation for time span 30 days, 45 days and 60 days at $30^0$C. The following parameters were

**5)** Table no.18. Stability study of Nanoparticle based gel

| **Parameters** | **Time span in days** | | |
|---|---|---|---|
| | **30** | **45** | **60** |
| pH | 4.4±0.120 | 4.5 ±0.124 | 4.3 ±0.157 |
| color | Yellowish white | Yellowish white | Yellowish white |
| % drug content | 96.10±1.12 | 93.98±0.921 | 91.30±1.36 |

**Mean ±SD; n=3**

It could be concluded that the prepared nanoparticle based gel formulation was stable. It is also observed that, day by day the elasticity of gel base was slightly lowers but it may not interfere with the stability of nanoparticle based gel formulation.

## IV. SUMMARY AND CONCLUSION

Summary of the present work accomplished:

After topical application to the skin of normal subjects, systemic absorption of Bifonazole is extremely low. As well as the topical applications of the Bifonazole are very few due to its poor penetration ability. This study is done to increase the dermal absorption of Bifonazole and it proves that Bifonazole can be effectively used in fungal treatment. Pharmaceutically acceptable, non- irritating and non-sensitizing excipients were selected. From pseudo ternary phase diagram, the concentration of oil phase; Smix distilled water were optimized and further processed for the formulation of Bifonazole Nanoparticle and nanoparticle based topical gel. Suitability and nature of gel formulation was studied with parameters like pH, Drug release, Spreadability and rheological characterization which showed that gel prepared was stable and viscoelastic in nature.

Permeation rate of Bifonazole through dialysis membrane was studied by Franz diffusion cell which confirmed that drug can easily permeate through artificial membrane due to small globule size of nanoparticle, nature of excipients used (Oleic acid, Acrysol k 150, Cremophor EL, Ethanol) and mechanism of nanoparticle. In vitro studies of drug molecule was done by anti- fungal activity study which indicates that effect of drug was enhanced by prepared nanoparticle based gel

## V. CONCLUSION

From the present study, It was concluded that,

1) Both nanoparticle and nanoparticle based gel made up of biocompatible constituents like Oleic acid,Acrysol k150, Cremophor EL and ethanol showed increased and controlled drug permeation.

2)

3) From rheological measurement, it was found that optimized NBG 2 formulations were highly stable,

viscoelastic, having good flow property, good spreadability and applicability.

4)

No irritation, no toxicity and ease of application with the use of biocompatible ingredients such as oleic acid, Acrysol K150 Cremophor EL, ethanol for formulation of Nanoparticle based gel.

Due to the structure of physicochemical properties of Nanoparticle and Carbopol 934 being Bioadhesive polymer it will fuse with skin membrane and facilitate drug delivery.

The superior flux was observed mainly due to the large solubilizing power of nanoparticle, which leads to large concentration gradient towards target site. The absorption of drug from nanoparticle depends on the mean size of the oil phase droplets and on the vehicle constituents.
From in vitro studies, it was concluded that nanoparticle and nanoparticle based gel formulation has better antifungal and prolonged activity.

Stability study suggested that Bifonazole loaded nanoparticle and nanoparticle based gel formulation was stable at all conditions.

The present study confirms that the topical application of Bifonazole can be effective in skin treatment and also nanoparticle based gel can improve the therapeutic efficacy of poorly water soluble drugs like Bifonazole . Gel can sustain the release for 24 hrs. The release of the Bifonazole revealed that Formulation have slower drug release at the start and it will sustain due to bioadhesion to the infectious skin membrane

## RECOMMENDATION

Future perspective of present work is:

Formation of Self nanoemulsifying DDS (SMEDS) of Bifonazole can be possible. Conversion of SMEDS of Bifonazole into suitable dosage form can be more effective antifungal treatment. Stability study of formulation can be studied. We can modify the formulation by using advanced polymer that can be act as both like emulsifying as well gelling properties like pemulen.

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