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# Formulation and evaluation of herbal nanogel of butoconazole for vaginal infection

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**Abstract**
The present study aims to formulate butoconazole herbal nanogel as the available dosage forms of drug have low bioavailability due to its poor solubility. The herbal nanogel prepared would overcome this drawback as particle size is reduced and first pass metabolism of drug is avoided in this type of dosage form. Moreover to formulate herbal ingredients are used which will have no side effects. In this study we have prepared nanoparticles of cinnamon aldehyde extract and lemon grass oil by nanopercipitation method and incorporated them into a gel by dispersion method. F1 Formulation was found to be best one as it showed all positive results during evaluation studies. The prepared formulation were evaluated for following parameters like physical examination, particle size, viscosity, Ph, spread ability, drug content and in-vitro drug diffusion test.

**Keywords:** Butoconazole, nanogel, nanopercipitation, dispersion method

## Introduction
Nowadays its a challenging to formulate the accurate dosage form of drug. Therefore in this present research work DOE software is used to select the formulation ingredients used to prepare nanoherbal gel of butoconazole drug so that side effects can be reduced and drug bioavailability can be enhanced by formulating suitable dosage form [1]. Nanogel formulations, are set as boon are delivering drugs to target organs. These formulation also have power to change or alter drug profile, pharmacokinetic and dynamic parameters by improving patient safety and compliance [2].

Nanogels, are considered as a nano size medicinal products which offer stability, strong permeation power due to reduced size, have biological consistency which help gel to stay for longer period of time to target area [3] Nanogels are advantageous over variety of prominent sectors, like gene delivery, chemotherapeutic,, diagnostics, organ targeting, and herbal medicines etc [4] Few years ago nanogels have increased their applications in other sectors like biotechnology, majorly used in dealing with genetics, protein synthesis, and enzyme immobilization [5].

In present research herbal extract of natural ingredients like cinnamon aldehyde and lemon grass oil nanoparticles were formulated which help to increase bioavailability by decreasing size and enhancing solubility. Cinnamon aldehyde possess antifungal properties, and lemongrass contains citral that have antimicrobial and anti-inflammatory effects therefore they are used with drug butoconazole and incorporated into gel to form nanogel which will have more absorption power as it would directly applied to targeted side and would have fewer side effects as compared to other dosage form [6].

In present research, 12 Nano gel formulations of butoconazole extract (1% w/w) in the form of butoconazole nanoparticles were formulated and evaluated. Than nanogel was evaluated for viscosity, pH of the formulation, spread ability, *in vitro* drug diffusion, and drug permeation [7] The results founded a novel and useful approach to design nanogel formulation where the active ingredient shows the optimum result [8]

## Material and Equipments Used

**A) Materials used**

| S. No | Ingredients |
|---|---|
| 1. | Butoconazole |
| 2. | Cinnamon extract |
| 3. | Lemon grass oil |
| 4. | Chitosan |
| 5. | Acetic acid |
| 6. | TPP |
| 7. | Carbopol |
| 8. | Methanol |
| 9. | Ethanol |
| 10. | Distill water |

**B) Equipments used**

| S. No | Equipments |
|---|---|
| 1. | Weighing balance |
| 2. | Hot air oven |
| 3. | UV-spectrophotometer |
| 4. | Dissolution apparatus |
| 5. | Magnetic stirrer |
| 6. | Brookfield viscometer |
| 7. | Franz diffusion cell |

**Method of Preparation**

**A) Preparation of herbal nanoparticles**

Butoconazole herbal nanoparticles were prepared using nanoprecipitation method. Accurately weighed drug and herbal extract of cinnamon (cinnamon aldehyde obtain from cinnamon barks) and lemon grass oil were dissolved in acetic acid & chitosan on magnetic stirrer. Sodium tripolyphosphate (TPP) (5 percent) was incorporated to above mixture dropwise at a uniform rate by syringe. Than mixing was done for 2 hrs followed at 13000 rpm by centrifugation for 5 minutes. The supernatant was discarded, and the pH 6.8phosphate buffer nanoparticles were suspended again. Than centrifugation was done at 15000, nanoparticle were extracted and the obtained pellet was washed three times with filtered water and nanoparticles were obtained [9].

**Table 1:** list of ingredients used to prepared herbal nanoparticles

| S. No | Ingredients used | N1 | N2 | N3 | N4 | N5 |
|---|---|---|---|---|---|---|
| 1. | Butoconazole (%) | 5 | 5 | 5 | 5 | 5 |
| 2. | Cinnamon extract (%) | 2 | 2 | 2 | 2 | 2 |
| 3. | Lemon grass oil (ml) | 1 | 1 | 1 | 1 | 1 |
| 4. | Chitosan | 0.35 | 0.54 | 0.75 | 1 | 1.25 |
| 5. | Acetic acid | 2 | 2 | 2 | 2 | 2 |
| 6. | TPP | 1 | 1 | 1 | 1 | 1 |

**B) Formulation of nanoherbal gel**

Nanoherbal gel was formulated using dispersion method. Carbopol 194 was dispersed in water for 2 hours. Once it got swelled mixture was stirred on magnetic stirrer he prescribed amount of butoconazole loaded nanoparticles were added to the dispersion to bring 1% of the substance into the gel, together with propylene glycol and glycerine were injected into the mixture and stirred at 500rpm using a magnetic stirrer. Stirring continued until the Carbapol 934 was completely dispersed to obtain the homogeneous gel. To shape an attractive gel formulation, the final pH was changed to 6.1-6.8 by adding triethanolamine [9].

**Evaluation of Herbal Nanogel Formulation**

**I) Evaluation of Nanoparticles**

**a) Particle Size and PDI:** Laser scattering zetasizer was used to measure particle size of formulations. There were twelve measurements, and the average was determined [10].

**II) Evaluation of cinnamon aldehyde and lemon grass oil Nanoparticles Loaded Nano gel**

**a) Physical examination:** The prepared Nanogel formulation was inspected visually for its colour, appearance and consistency [11].

**b) Measurement of viscosity:** The viscosity of Nanogel was measured using the Brookfield DV-III Rheometer The C-14 spindle was attached to the Brookfield Rheometer. The spindle was inserted into the sample holder with a dip in the topical Nanogel. Then the holder of the sample was connected to the instrument and measured the viscosity of the topical nanogel [11].

**c) Measurement of spreadability:** Using two glass slides (6 cm2), the spreadability of the Nanogel was measured. Every batch of 0.4 g topical Nanogel was put between two slides and left for 1 min. The diameter of the topical nanogel spread circle was measured and compared with each other. [12]

**d) Homogeneity test:** Visual inspection was performed, to test homogeneity. In order to check whether the prepared topical nanogel was homogeneous it was cheched that all formulations should not contain lumps or aggregates [12]

**e) Drug content or drug uniformity:** Nanogel was dissolved into the 50 ml of methanol. To dissolve into the methanol, it was sonicated for 15 min. The solution was filtered through the Whitman filter paper and methanol was diluted with the resultant filtrate. Using UV visible spectroscopy and drug material, the aliquot subjected to 271 nm wavelengths scanning was measured [13]

**f) Extrudability test:** The formulations were transfered in the collapsible tube after nanogels were poured in the pipe. The formulation extrudability was calculated in terms of the weight into grams needed for the 0.5 cm ribbon gel to be extruded in 10 seconds.

**g) FTIR Studies:** Compatibility study were done using Perkin Elmer Fourier transformation Infrared spectroscope in the range of 4000 cm-1 to 400 cm-1. Potassium Bromide Pellet was prepared by applying pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in light path and the spectra were analysed [13]

**h) In-Vitro Drug Diffusion Studies:** Using a Franz diffusion cell apparatus, the in-vitro drug diffusion of Nanogel of all formulation was studied. the dialysis membrane was soaked in the phosphate buffer of pH 7.4. 0.4g of Nanogel was placed in the donor compartment and then pH 7.4 phosphate buffer was filled into the receptor compartment. The dialysis membrane was used as a diffusion membrane between the donor and the receptor compartment and the use of the clamp remained tight. Using the Teflon coated stirring the bar, the receptor compartment media temperature was held at 37 °C (± 0.5 °C) below 100 rpm. At each prefixed time interval of 1, 2, 3, 4, 5 and 6h, 3ml aliquots was collected and sinks condition was preserved over a period of full diffusion analysis. Using UV

at wavelength 271 nm, the collected aliquots were scanned and the percentage of cumulative drug release of Nanogel was calculated [14].

## Result and Discussion

### a) Physiochemical evaluation of butoconazole drug

| S. No | Parameters | Description |
|---|---|---|
| 1. | Colour | White |
| 2. | Description | Imidazole antifungal drug |
| 3. | Odour | Odourless |
| 4. | Form | Slightly crystalline powder |
| 5. | Melting point | 159 °C |

### b) Solubility profile of butoconazole drug

| S. No | Solvent | Solubility observation |
|---|---|---|
| 1. | Methanol | 0.14mg/ml |
| 2. | Ethanol | 0.25mg/ml |
| 3. | Water | 0.09mg/ml |
| 4. | DMF | 32mg/ml |
| 5. | DMSO | 30mg/ml |

**c) Determination of λ max of butoconazole:** In order to determine the maximum absorption, the formulated stock solution was scanned between 200 to 400 Nanometres. It was found to be 271 nm [15].

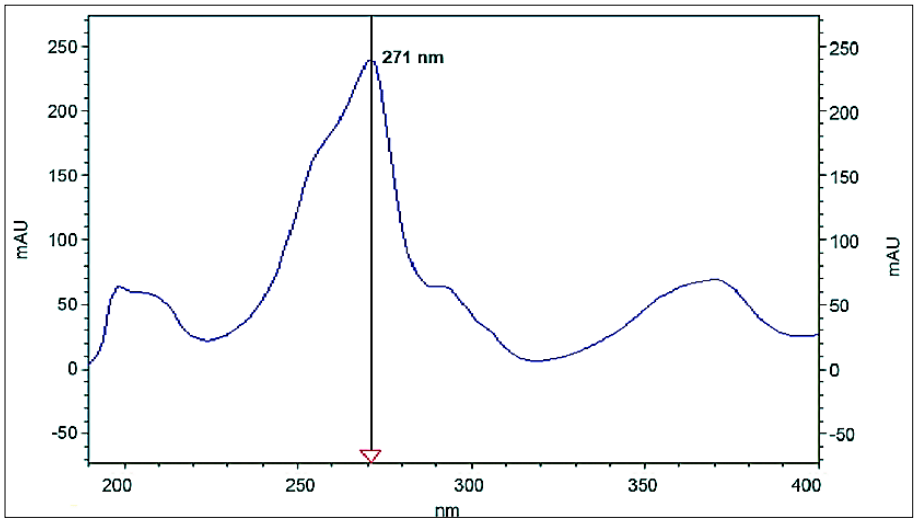



**Fig 1:** Lamda max determination of butoconazole

**d) Calibration curve:** The standard curve of butoconazole was obtained and good correlation was obtained with R2 value of 0.9995, the medium selected was pH 7.4 phosphate buffer [15].

| Concentration (µg/ml) | Absorbance |
|---|---|
| 0 (µg/ml) | 0 |
| 10 (µg/ml) | 0.1458 |
| 20 (µg/ml) | 0.2184 |
| 30 (µg/ml) | 0.3263 |
| 40 (µg/ml) | 0.4458 |
| 50 (µg/ml) | 0.5497 |

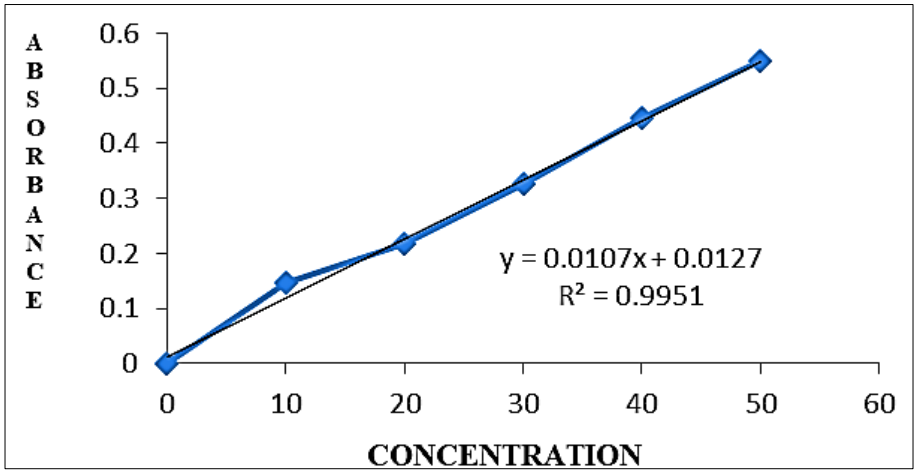
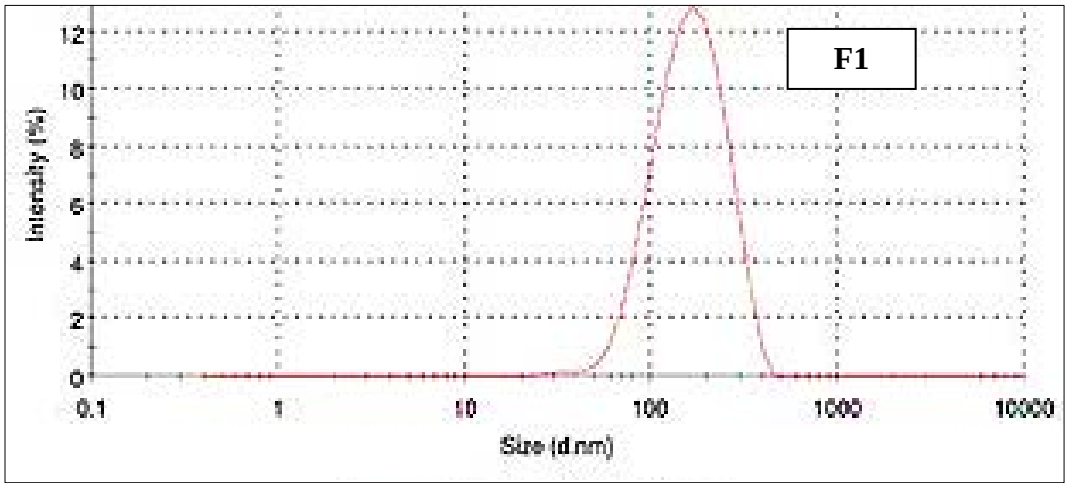


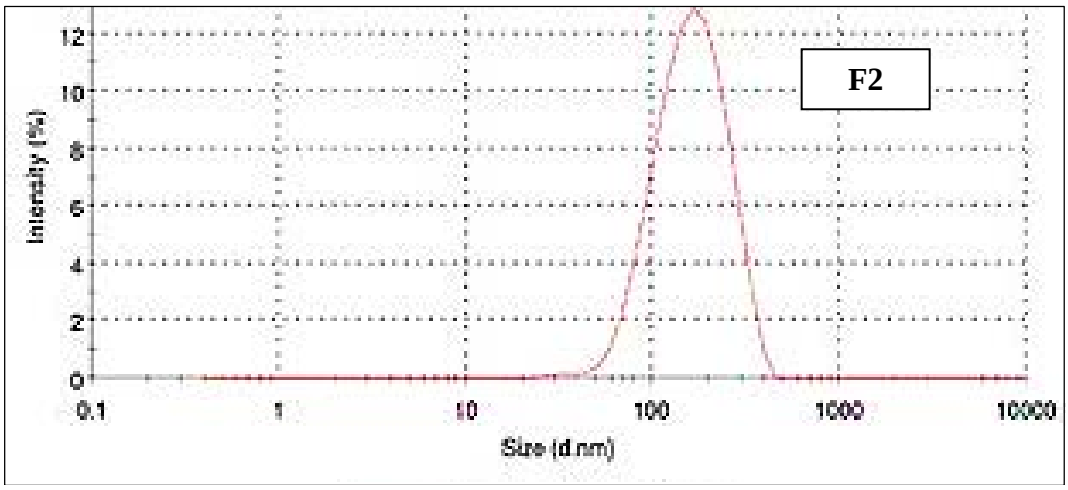

**Fig 2:** Calibration curve of butoconazole in phosphate buffer Ph 7.4

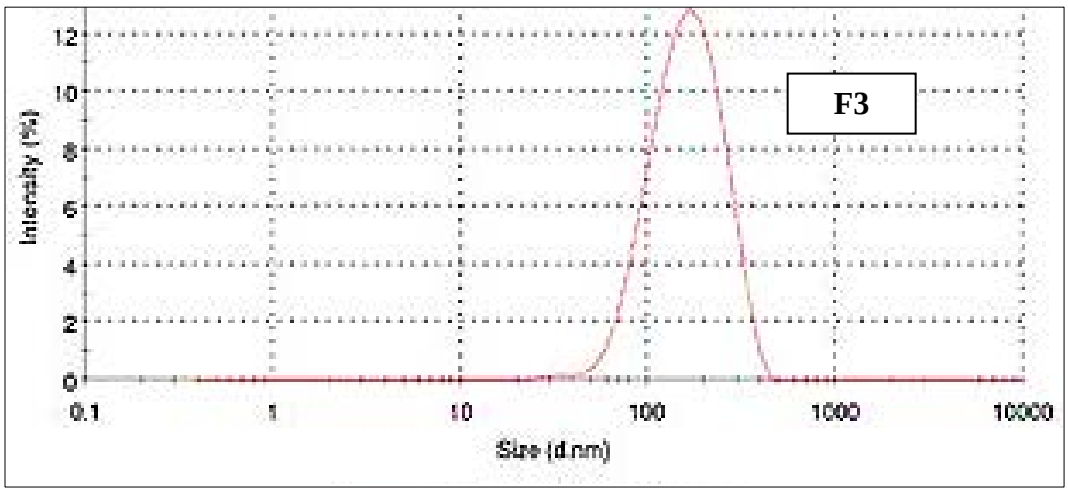
**e) Evaluation of nanoparticles:** The average size of nanoparticles was carried out by using zeta sizer. The maximum zeta potential of nanoparticle was found to be 40.6mV. the zeta potential was found to elevate with the particles surface charge. The results have also shown that the zeta potential was found to get an enhance with the

increase in particle surface charge. The average particle size and Zeta Potential of Nanoparticles was recorded in Table. The average particle size of nanoparticles was found to be 168.7 to 254.45 Nm [16]

| S. No | Formulations | Particle size (nm) | Zeta potential (mV) |
|---|---|---|---|
| 1. | N1 | 221.76 nm | +34.9 mV |
| 2. | N2 | 254.45 nm | +38.6 mV |
| 3. | N3 | 349.5 nm | +40.6 mV |
| 4. | N4 | 189.47 nm | +32.7 mV |
| 5. | N5 | 168.7 nm | +29.2 mV |



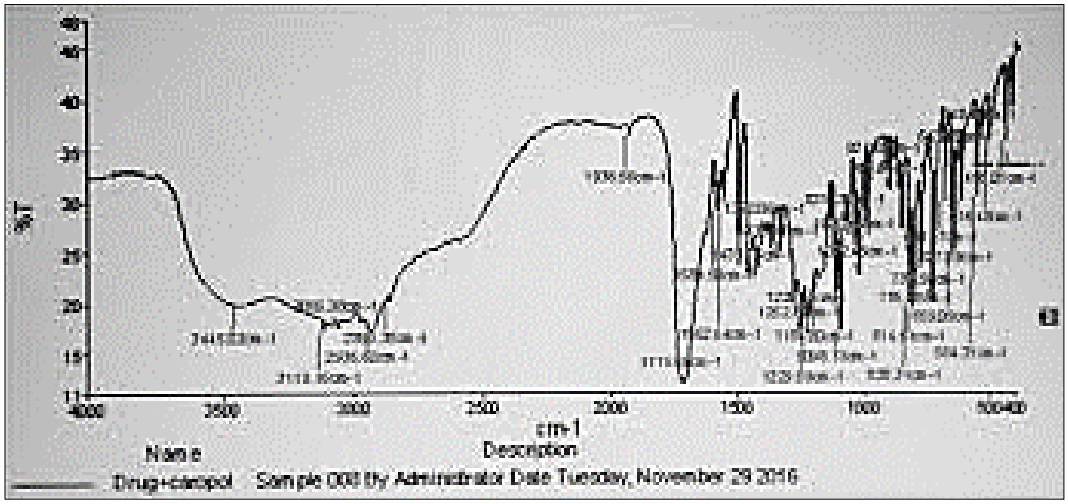




**f) Evaluation of Nanogel**

**1. Physical examination:** All formulations of Nanogel were evaluated for their physical properties such as colour, Texture and consistency. The prepared Nanogel was yellowish brown in colour with a pleasant, Smooth homogeneous appearance and texture.

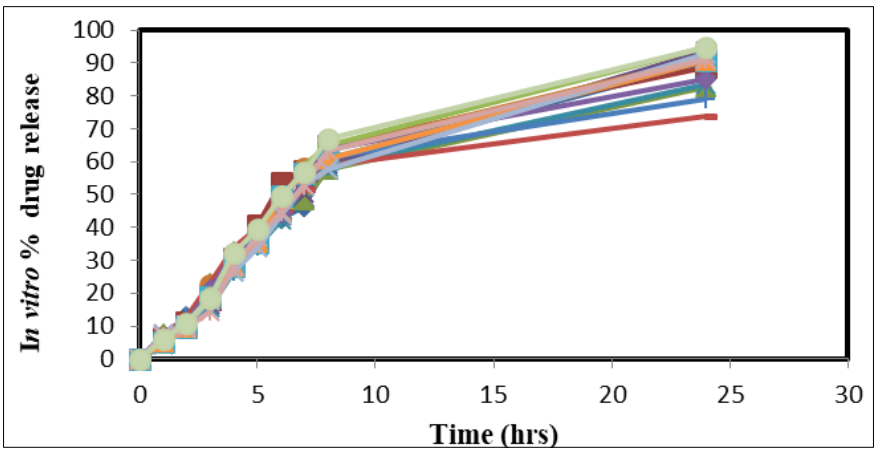
| S. No | Formulations | Physical examination results |
|---|---|---|
| 1. | F1 | +++ |
| 2. | F2 | + |
| 3. | F3 | + |
| 4. | F4 | ++ |
| 5. | F5 | + |
| 6. | F6 | + |
| 7. | F7 | + |
| 8. | F8 | ++ |
| 9. | F9 | + |
| 10. | F10 | + |
| 11. | F11 | + |
| 12. | F12 | + |

**2. FTIR studies-** The characteristic bands were identifiable and no major shifts were observed in formulation which indicates that the drug is intact in the formulation has not reacted with the excipients.




**3. *In vitro* drug Diffusion Studies:** Franz diffusion cell apparatus was used to record drug release of topical Nanogel formulation. The collected aliquots were scanned using UV-Visible spectrophotometer, and % cumulative drug release was calculated.

| S. No | Formulation code | % cummulative drug release |
|---|---|---|
| 1. | N1 | 92.34% |
| 2. | N2 | 69.73% |
| 3. | N3 | 59.6% |
| 4. | N4 | 89.50% |
| 5. | N5 | 78.7% |
| 6. | N6 | 63.54% |
| 7. | N7 | 57.345 |
| 8. | N8 | 85.21% |
| 9. | N9 | 70.9% |
| 10. | N10 | 83.09% |
| 11. | N11 | 75.06% |
| 12. | N12 | 67.8% |



**1. Drug content:** drug content of all formulation was determined and recorded in table no.

| S. No | Formulation code | % drug content |
|---|---|---|
| 1. | F1 | 95.87% |
| 2. | F2 | 77.2% |
| 3. | F3 | 80.06% |
| 4. | F4 | 88.30% |
| 5. | F5 | 69.43% |
| 6. | F6 | 73.5% |
| 7. | F7 | 60.94% |
| 8. | F8 | 89.1% |
| 9. | F9 | 78.55% |
| 10. | F10 | 92.% |
| 11. | F11 | 83.67% |
| 12. | F12 | 76.80% |

**2. Viscosity:** Nanogel viscosity was determined and results of formulation were recorded and were found to be between few 100-1000 centipoise.

**Summary and Conculsion**

The present study was carried out to formulate and evaluate the herbal nanogel formulation of butoconazole using cinnamon extract and lemon grass oil as the available dosage form of drug for vaginal infection have poor solubility and bioavailability therefore to overcome these drawbacks herbal nanogel formulation can be boon for this drug as particle size will be reduced, first pass metabolism would be avoided and moreover it would have no side effects as herbal ingredients are used to formulate it [17] The nanoparticles were first prepared using precipitation method and than incorporated into gel using dispersion method [18]. All formulation were evaluated for following parameters like physical examination, particle size, viscosity, Ph, spread ability, drug content and *in-vitro* drug diffusion test [19]. The best formulation was as values of all parameters were in good range of this formulation. In future this study data can be used to evaluate the formulation by performing pre-clinical studies [20].

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