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Formulation and evaluation of transdermal preparation of bifonazole for the treatment of Sabboric dermatitis

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Abstract--The current work marks a concentrate on definition plan and assessment of antifungal Cream. This study comprises of Bifonazole as unmistakable specialists for against candida or antifungal action. A few excipients, for example, Liquid paraffin and borax as emulsifying specialist were utilized to deliver critical definition as Cream. The Cream were ready by utilizing 3.5% Liquid Paraffin, Methyl Parabens and Propyl Parabens separately have their own OK outcomes as shown in the trial study. The pH of definitions was 6.20 to 5.90 and consistency according to Brook field viscometer 11 was in the scope of 95400-127200. Cream was truly assessed and found no totals aftereffects of which showed magnificent consistency. As far as spredibility the definition containing 3.5% blend of Liquid Paraffin has more worth (19.52±0.018) that promoted antifungal cleanser. Sound qualities boundary consideration of sped up steadiness according to standard method and based on standard worth in conditions of temperature and moistness was of huge outcomes. Miniature organic investigations were completed to decide antifungal testing of the two definitions of thought of zone of hindrance and least inhibitory fixation and it was found that Cream containing 3.5% mix of Liquid Paraffin had more enemy of candida action (ZOI is 35mm) and home grown showcased antifungal Cream (ZOI 45mm). From the above ordered information the concentrate plainly shows that the plan is showing great in-vitro enemy of parasitic movement against E.coli and candida albicans.

Keywords---sabboric dermatitis, transdermal, bifomazole.

Introduction

Transdermal Drug Delivery System

Drug delivery system (DDS) is a generic term for a series of physicochemical technologies that can control delivery and release of pharmacologically active substances into cells, tissues and organs, such that these active substances could exert optimal effects [1, 2]. In other words, DDS covers the routes of administration and drug formulations that efficiently deliver the drug to maximize therapeutic efficacy while minimizing any side effect TDDS does not involve passage through the gastrointestinal tract; therefore, there is no loss due to first-pass metabolism, and drugs can be delivered without interference from pH, enzymes, and intestinal bacteria. In addition, TDDS can be used to control drug release according to usage restrictions, thereby contributing to the high persistence of this method[3-5].

Advantages of TDDS

- Avoidance of 1st pass metabolism.
- Avoidance of gastro intestinal incompatibility.
- Predictable and broadened length of movement.
- Minimizing unfortunate results

Limitations of TDDS

- This course organization is unsatisfactory for drugs that bother or sharpen the skin.
- Transdermal course can't convey in a pulsatile design.
- Transdermal conveyance is either common sense nor reasonable when needed to convey huge portions of drug skin.

Materials and Methods

Bifonazole is gift sample form Adin pharma meerut, liquid paraffin, borax, Methyl Paraben, Propyle Paraben is purchase form College laboratories.

Preformulation Study

Melting Point

The Melting Point of Bifonazole was determined by Capillary Method. The melting Point was found to be in the range of 143-145°C.

Identification Tests By UV Spectrophotometry

Bifonazole 200mg was taken in a 100ml volumetric flask and volume was made up with methanol. 1ml of the solution was pipette out and diluted to 100ml with

methanol. Examined b/w 200-400 nm. The solution showed maximum abs. at 256.2nm.

FTIR Spectrum Study

A FTIR Spectrum of drug sample was taken by using kBr Pellet b/w 4000 – 500cm⁻¹. Spectra are as shown in fig and interpretations are shown in table .

Preparation of Antifungal Cream containing 3.5% Liquid Paraffin Procedure

- The ingredients were accurately measured or weighed as per the table.
- The water soluble components which come under aqueous phase were heated on water bath shaker at 75±1° Celsius in separate beaker.
- Oil soluble components which come under oil phase were also heated at 75±1° Celsius in separate beaker followed by addition of Liquid Paraffin (concentration 3.5%) in oil phase under constant stirring.
- Then to the heated aqueous mixture, oily phase was incorporated with incessant stirring on magnetic stirrer up to the emulsion cooled down.

Table 1
Formulae for Antifungal Cream

| S. No | Phase | Ingredients | F1 | F2 | F3 | F4 |
|-------|--------------|-----------------|------------|------------|------------|------------|
| 1 | Oil Phase | Bifonazole | 10 | 10 | 10 | 10 |
| | | Liquid Paraffin | 2 | 2.5 | 3 | 3.5 |
| 2 | Liquid Phase | Borax | 0.5 | 1 | 1.5 | 2 |
| 3 | | Methyl Paraben | 0.4 | 0.4 | 0.6 | 0.4 |
| 4 | | Propyl Paraben | 0.3 | 0.3 | 0.4 | 0.2 |
| 5 | | Perfume | Q.s | Q.s | Q.s | Q.s |
| 6 | | Water | Up to 20ml | Up to 20ml | Up to 20ml | Up to 20ml |

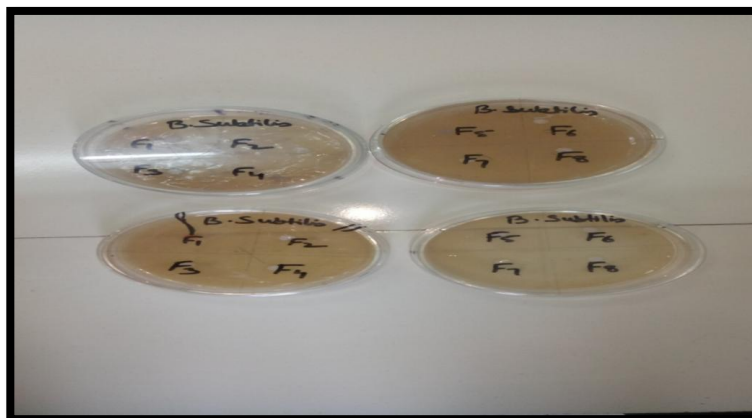


Fig 2. Prepared Antifungal Cream

In-vitro Evaluation of Antifungal Cream: pH Determination

pH of Cream of various concentrations was measured by a digital pH meter calibrated bath std. buffer solution having pH 4.0 and pH 7.0. about 5gm, of Cream was weighed and transferred into 100 ml beaker into which 45 ml of distilled water was transferred and pH was determined at 25 degree Celsius temperature.

Viscosity

In order to determine the viscosity values, viscosity measurements were performed by using rotational viscometer DV-III Ultra (Brook field engineering laboratories) Speed of rotation at 20 RPM and measurements were performed at 22 degree Celsius temperature by using spindle.

Spread Ability Studies

A significant criterion for semisolids is that they have a strong propagation power. It is a concept expressed to represent the degree to which, when applied to the hair, the shampoo easily spreads the therapeutic effectiveness of the semisolid topical formulation also depends in a large extent on its spread ability benefit. The basic apparatus was designed to assess semi-solids formulations spread ability, however. Spread ability is often defined as the time taken in sec. by two slides to slip away from formulation that is put amid two slides under the application of a definite load. It has been shown that the shorter the time needed to separate the two glass slides the better the spread ability or spread value. Two glass slides of normal & defined dimensions were chosen, and over any each of the slides was placed the prepared formulation whose spread ability had to be calculated. Then the other one was put on uppermost surface of the formulations that were sandwiched along the slide between the two slides that were 5 cm long. By putting a weight of 100 gm on the upper slide, a uniform thin layer of antifungal Cream (semi-solid formulation b/w, two slides) was obtained. The weight was then stripped and the surplus of Cream clinging to the slides was scrapped off. One of the glass slides on which the Cream was mounted was fixed and the second movable glass slide was positioned over it. A string to which specified load could be applied using a simple pulley and a pan was connected to the one end of the second movable slide. A weight of 30 gm was placed on the pan and the time taken to travel the distance of 5.0 cm for the upper movable slide and detach it from the lower one slide under the direction of the weight applied was noted. The formula given the spread value was then determined.

$$\text{Spread ability} = m \times l / t$$

Where,

M = weight tied to the upper slide (30g)

L = length of glass slide (5cm)

T = time taken in seconds

Self-Irritancy Patch Test

The area of 1 square cm on the dorsal surface of left hand was marked. The Cream was applied under a cotton patch to the stipulated area and time was noted. Irritation, erythema and edoema were examined, if any, at regular intervals of up to 24 hours and recorded.

% Drug Content

Bifonazole 200mg was taken in a 100ml volumetric flask and volume was made up with methanol. 1ml of the solution was pipette out and diluted to 100ml with methanol. Then aliquots were further diluted with methanol to get conc. 5, 10, 15, 20 & 25µg/ml. Absorbance were recorded spectrophotometrically at 256.2nm.

Microbiological Studies

Antifungal Testing of Cream

Preparation of Media

To assets the in vitro operation, Sabouraud's Dextrose Broth was used the media has been prepared as per manufacturer's instructions. Using a weighing balance, about 19.5grams of Sabouraud Dextrose Agar (SDA) was weighed and dissolved into a conical flask containing 300 ml of distilled sterile water. Then it was shaken. Mixed and dissolved in a hot dish. The pH of same was changed as needed. The media was then placed in an autoclave for sterilization at a pressure of 15lbs at 121 °Celsius or 15 minutes. The media was then allowed to cool down to approximately 45 °C and then poured into petri plates which are previously sterilized. Then plates were allowed overnight to solidify. For further use, the plates were then held at 4 °C

In vitro Drug Diffusion

A glass cylinder with both ends open, 10cm height, 3.7cm outer diameter and 3.1cm inner diameter was used as permeation cell. A cellophane membrane prehydrated in pH 7.4 buffer (24hrs. before use) was fixed to one end of the cylinder with the aid of an adhesive to result in permeation. One gram of semisolid formulation was taken in the cell (donor compartment) and the cell was attached to a beaker containing 140ml of drug-free pH 7.4 phosphate buffer as receptor compartment. The medium in the receptor compartment was agitated using a magnetic stirrer and a temperature of 37°C±1°C was maintained. Samples of 1 ml from the receptor compartment were taken at various intervals over a period of 3 h with replacement of an equal amount of drug-free buffer (7.4 Phosphate). The samples were estimated by measuring the absorbance at 256.2nm in a UV-1700 Shimadzu spectrophotometer [75, 76].

Marketed Formulation

Determination of Minimum Inhibitory Concentration (MIC)

There no apparent turbidity is observed in the test tube, MIC is classified as the lowest concentration. In this process, the technique of broth dilution was used where formulations were prepared in sterile DMSO at the maximum

concentration of 50 $\mu\text{g/ml}$ and serially calculated to a working concentration varying from 10 $\mu\text{g/ml}$ to 50 $\mu\text{g/ml}$ using SD broth forgen and then inoculated with 40ml suspension of the test species. Test tubes were noted for Turbidity after 24 hours of incubation. The lowest concentration was determined and noted MIC if no turbidity was observed.

Stability Testing

Stability testing is one of the most important parameter which begins with discovery of drug product and ends with demise of commercial product. ICH guidelines were followed to carry out stability testing of antifungal Cream. The prepared Cream was filled in sterilized container and kept in humidity chamber & maintained at 30-2 Celsius/ 65 \pm 5% Relative Humidity and 40 \pm 2 $^{\circ}$ Celsius/75-5% Relative Humidity for 3-months. At the end samples were examined for the Organoleptic characters and viscosity too.

Results

Preformulation Study

UV Spectrophotometry

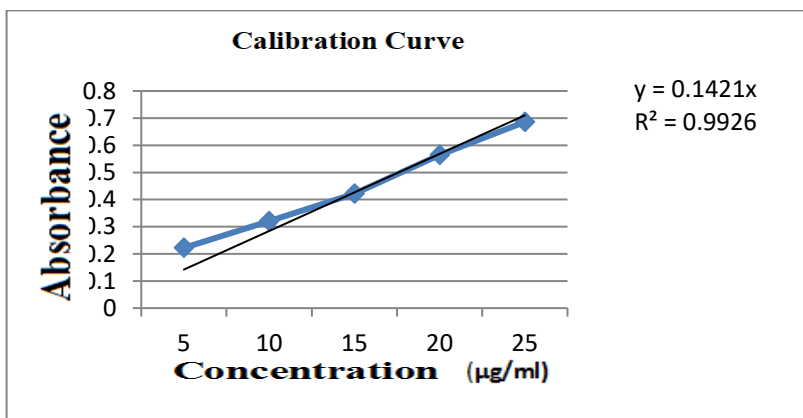


Fig 3.1. Standard Calibration Curve of Bifonazole in Methanol

FTIR Spectrum Study

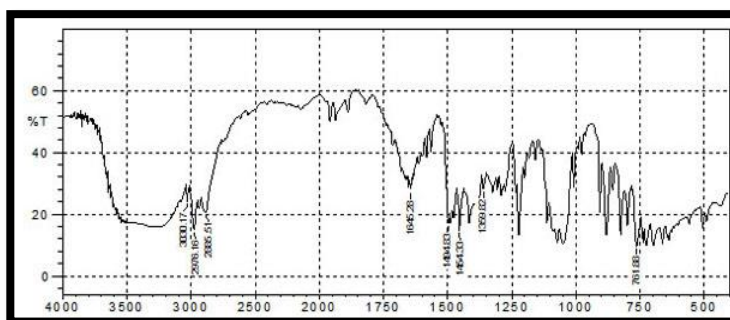


Fig 3. FTIR Spectra of Bifonazole Sample

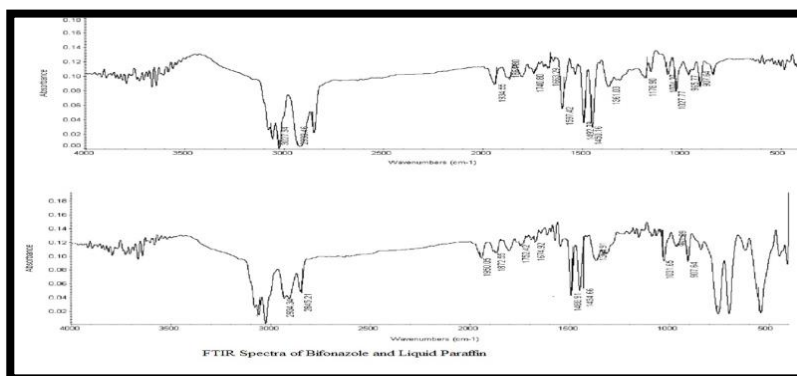


Fig 4. FTIR Spectra of Bifonazole Sample and Liquid Paraffin

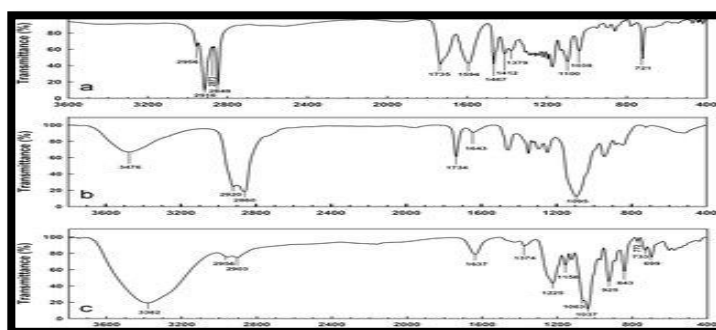


Fig 5. FTIR Spectra of Bifonazole Sample & Methyl Paraben, Borax

In-vitro Evaluation of Antifungal Cream

Table 4
In-vitro Evaluation of Antifungal Cream

| Formulation Code | pH | Viscosity Centipoise | Spread Ability | Self-Irritancy | % Drug Content |
|------------------|------|----------------------|----------------|----------------|----------------|
| F1 | 6.20 | 95400 | 24.10±0.032 | No | 97.95±0.012 |
| F2 | 6.10 | 98300 | 22.28±0.042 | No | 97.10±0.035 |
| F3 | 6.02 | 101200 | 21.56±0.032 | No | 99.86±0.016 |
| F4 | 5.90 | 127200 | 19.52±0.018 | No | 98.75±0.046 |

Microbiological Studies Antifungal Testing of Cream

From the microbial study it was found that the cream showing good effects on microbial growth and the zone of inhibition was calculated by zone reader. The zone of inhibition of candida albicans was 38.24mm, 39.86mm, 42.40mm and 41.30mm & E.coli it was 28.34mm, 30.56mm, 34.42mm & 33.62mm.



Fig 6. against Candida Albicans



Fig 7. Against E.coli

Table 5
Microbiological Studies

| Formulation Code | Zone of inhibition | |
|------------------|--------------------|---------|
| | Candida Albicans | E.Coli |
| F1 | 38.24mm | 28.34mm |
| F2 | 39.86mm | 30.56mm |
| F3 | 42.40mm | 34.42mm |
| F4 | 41.30mm | 33.62mm |

From the above compiled data the study clearly shows that the formulation is showing good in-vitro anti-fungal activity against E.coli and candida albicans.

In vitro Drug Diffusion

Table 6
In vitro Drug Diffusion

| S.No | Time Interval (min) | F1 | F2 | F3 | F4 |
|------|---------------------|-------|-------|-------|-------|
| 1 | 30 | 30.84 | 31.51 | 30.02 | 31.08 |
| 2 | 60 | 46.92 | 47.25 | 45.72 | 44.27 |
| 3 | 90 | 60.34 | 61.52 | 58.62 | 62.74 |
| 4 | 120 | 74.45 | 72.93 | 73.34 | 71.18 |
| 5 | 150 | 82.62 | 81.35 | 84.76 | 83.63 |
| 6 | 180 | 92.76 | 94.44 | 97.90 | 96.90 |

Minimum Inhibitory Concentration

Both designed formulation was evaluated for their MIC and compared with herbal marketed antifungal formulation. No turbidity was found at 25µg/ml for G1 and 20ug mi for F3 which subsequently compared with herbal marketed formulation had MIC at 40g ml further more results were demonstrated in table.3.7.

Table 7
Minimum Inhibitory Concentration

| FORMULATION | MIC |
|----------------------|---------|
| F1 | 15µg/ml |
| F2 | 25µg/ml |
| F3 | 28µg/ml |
| F4 | 35µg/ml |
| Marketed Formulation | 45µg/ml |

Stability Study

We have observed the formulation for 12 week and view the change or variation in the formulation. It was conclude from the stability studies there is no major variation in the color, pH, thermal stability viscosity and % Drug release.

Conclusion

From this investigation, it was concluded that both formulations has produced magnificent activity against fungal agents (candida albicans in this experimental study) but Cream containing 3.5% Liquid Paraffin has more prominent then other one and also than marketed antifungal formulation, Grounded on the results from the experimental study further usefulness of the dosage form might depend on pharmacokinetic data. Forthcoming or subsequent research work of antiviral activity. The formulation of the antifungal agent Bifonazole exhibited anenhanced rate of diffusion and anti-activity. The results of different chemical and physical tests of cream showed that it could use topically in order to protect against skin infections caused by fungus.

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