



FORMULATION AND EVALUATION OF MICONAZOLE NITRATE SOAP STRIPS FOR DERMAL INFECTIONS

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ABSTRACT

In present study, antifungal paper soap strips of miconazole nitrate were prepared & evaluated for dermal infections because the presence of thick foam on the infected part causes hydration of stratum corneum for better penetration of drug. The formulation and evaluation of medicated soap strips were carried out in two phases. Phase-I studies optimization, which was carried out to study water absorption capacity using different types of papers (Whatman filter paper no. 1, 41 and 42, filter paper, bond paper and butter paper) by determining the parameters weight gain, size, shape and foam test. From these parameters best soap, concentration of liquid soap solution and papers were selected. Phase-II studies involve incorporation of drug in best soap solution and papers chosen from phase-I studies. The medicated soap strips were prepared by dipping the selected paper in drug containing soap solution. The prepared medicated paper soap strips were characterized for weight gain, foam test, drug content uniformity, FTIR, in vitro drug release studies using diffusion cell with hydrated cellophane membrane and primary skin irritation test. The microbial studies indicate drug activity by zone of inhibition against microorganisms *C.albicans*, *S.typhi*, *S.aureus*, *E.coli*, *B.subtilis* and *A.niger* species. The obtained results for prepared medicated soap strip of Miconazole nitrate indicate that these strips are economic, convenient, gives good foam on application, uniform in drug content and not showing any skin irritation.

Keywords: Dermal infections, Miconazole nitrate, Thick foam, Hydration of stratum corneum, Medicated paper soap strips.

INTRODUCTION

Miconazole [(*RS*)-1-(2-(2,4-Dichlorobenzyloxy)-2-(2,4-dichlorophenyl)ethyl)-1*H*-imidazole] is an imidazole antifungal agent, commonly applied topically to the skin or to mucus membranes to cure fungal infections. It is highly efficacious drug for tinea, pityriasis versicolor, otomycosis and vulvovaginal candidiasis. It works by inhibiting the synthesis of ergosterol, a critical component of fungal cell membranes. It can also be used against certain species of *Leishmania* protozoa which are a type of unicellular parasite that also contain ergosterol in their cell membranes. In addition to its antifungal and antiparasitic actions, it also has some limited antibacterial properties. Topical formulations generally contain 2% miconazole nitrate¹⁻⁴.

Presence of thick foam on the infected part causes hydration of stratum corneum for better penetration of drug⁵⁻⁸. Topical drug delivery systems are available including medicated soaps having disadvantages like their economy, wastage, no accurate dosage, no proper foam formation etc. Hence the aim for present work was to prepare medicated soap strips which will be more effective against dermal infections.

MATERIALS AND METHODS

Materials

Miconazole nitrate was obtained from Nicholas Piramal as a gift sample. Soap X & soap Y were purchased from local market. Filter paper & Whatman filter paper no. 1, 41 & 42 were from New Neeta chemicals. Butter paper & bond paper were purchased from local market.

Methods

Phase 1

Selection of soap solution

Two non-medicated soaps of different brands were selected and coded as X and Y. Soap solution of varied concentration (5, 10, 15, 20% w/v) were prepared. Formation of foam was avoided during solution preparation. Foam test was the criteria for selection of good soap. The soap capable of producing maximum foam was selected.

Selection of paper

Six different branded papers (Whatman filter paper no. 1, 41 and 42, filter paper, bond paper and butter paper) were selected and coded as A, B, C, D, E, and F. They were evaluated for their absorption capacity and weight gain. The paper showing maximum absorbing capacity was considered as the best paper.

Formation of non medicated paper soap strips

The paper soap strips were prepared by Dipping technique using modified disintegration apparatus and air dried overnight at 37±2°C. For this purpose different papers were dipped one after another into the soap solution of varied concentration (5, 10, 15, 20% w/v) and air dried overnight.

Evaluation of non-medicated paper soap strips

The prepared strips were subjected for determination of size, shape, weight variation, pH and foam test by a reported standard method and an average of 20 strips was taken.

Phase 2

Formulation of medicated paper soap strips

The drug was incorporated in the selected formulation which showed good absorption capacity in phase-I studies. Accurately weighed drug (2% miconazole nitrate) was mixed with 15% soap powder and distilled water was added under constant and continuous stirring until a uniform soap-drug solution was formed. Then paper soap strips were prepared.

Table 1: Formulation of miconazole nitrate soap strips

Sr. No.	Ingredients	Quantity taken
1	Soap Y	15 gm each
2	Miconazole nitrate	2 gm
3	Distilled water	100 ml

Evaluation of paper soap strips

These prepared medicated soap strips were evaluated for weight gain, foam test, pH, in vitro drug release and primary skin irritation test. Microbial studies have been done by using microorganisms like *C.albicans*, *S.typhi*, *S.aureus*, *E.coli*, *K.pneumoniae*, *P.aeruginosa*,

B.subtilis and *A.niger* species. The % drug content is measured by using UV spectroscopy at λ_{max} 225 nm.

In vitro drug release⁸⁻¹¹

In vitro drug release of miconazole nitrate from prepared soap strips was studied by using Keshary-Chien diffusion cell. Prehydrated Cellophane paper was used as a membrane in this study. The study was done by using 0.1 N HCl media. The samples were collected at the interval of 3 minutes for a period of 15 minutes. The drug content was estimated by measuring the absorbance at 225 nm.

% Drug content

The % drug content is measured by using UV spectroscopy at λ_{max} 225 nm.

Primary skin irritation test

For this, three human volunteers were selected and the prepared soap strips were given to them and checked for irritation.

Microbial study¹²⁻¹⁴

Microbial study has been done using microorganisms such as *C.albicans*, *S.typhi*, *S.aureus*, *E.coli*, *K.pneumoniae*, *P.aeruginosa*, *B.subtilis* and *A.niger* species. For measuring the effectiveness of an

antimicrobial agent against fungi/bacteria grown in culture, the microorganism of interest was swabbed uniformly across a culture plate. Then a soap strip of 5×5 mm was placed on the surface of the agar. Then the plates were placed in incubator for 24 hrs at 30°C. The drug diffuses out from the paper soap strip into the agar. The concentration of the compound will be higher next to the strip, and will decrease gradually as distance from the strip increases.

IR spectral analysis for drug-excipient interaction¹⁵

The studies were carried out using IR method with the help of IR (Varian) spectrophotometer.

RESULTS AND DISCUSSION

Non-medicated soap strips

From the several papers studied the papers coded A, B and F found to have optimum absorption capacity. The solution of 15% Y soap was found good. All the strips have pH near about 7.0.

Medicated soap strips

The medicated soap strips found uniform in drug content, weight variation was found to be in the range and foam produced was ranging from 10 to 15 ml. The 15% soap solutions gave best results for foam, weight gain, pH and uniformity of soap distribution.

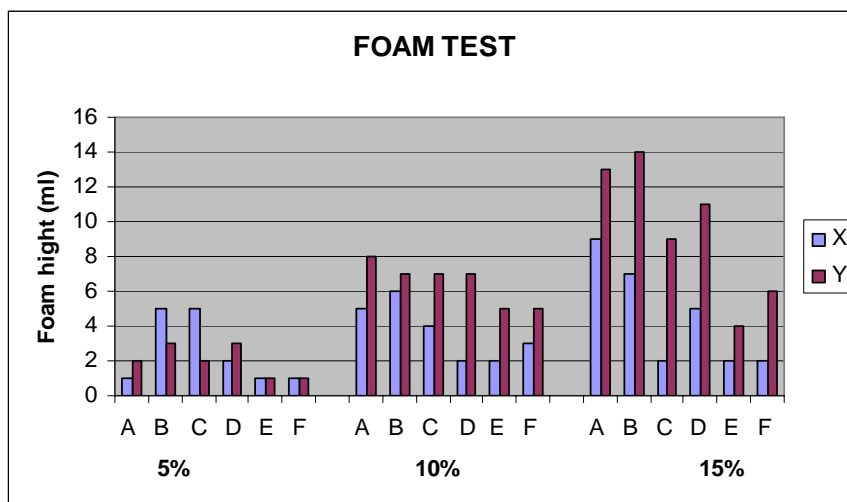


Fig. 1: Foam height produced by different non-medicated paper soap strips

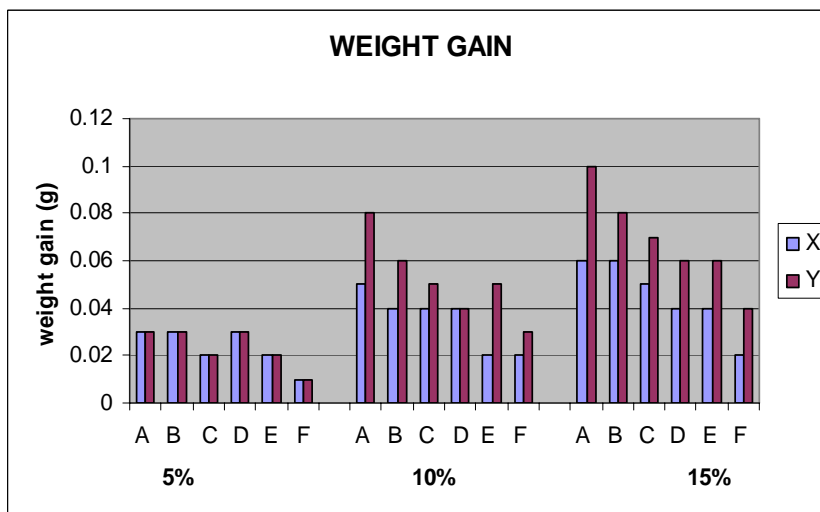


Fig. 2: Weight gain of different non-medicated paper

Table 2: Evaluation parameters of miconazole soap strips

Sr. No.	Parameters	2% Miconazole soap strips
1.	Weight variation	0.1 ± 0.01 gm
2.	Foam height	15 ± 0.00 ml
3.	% drug content	95 ± 5.0 %
4.	pH	7.0

In vitro drug release

In vitro drug release studies show the 100% drug released within 10 minutes.

Primary skin irritation test

Primary skin irritation test showed none of the medicated soap strip produces irritation.

Microbial study

Microbial study has been done using microorganisms such as *C.albicans*, *S.typhi*, *S.aureus*, *E.coli*, *K.pneumoniae*, *P.aeruginosa*, *B.subtilis* and *A.niger* species. It gave zone of inhibition against microorganisms *C.albicans*, *A.niger*, *S.typhi*, *S.aureus*, *E.coli* and *B.subtilis* species. It did not show any zone of inhibition against micro-organisms *K.pneumoniae* and *P.aeruginosa*. The diameter of zone of inhibition obtained in microbial testing by different strips against various micro-organisms is given in table below:

Table 3: Zone of inhibition obtained in microbial studies

Sr. No.	Micro-organism	Diameter of zone of inhibition(cm)		
		Strip A	Strip B	Strip F
1	<i>A.niger</i>	1.6 ± 0.1	2.4 ± 0.2	2.1 ± 0.2
2	<i>C.albicans</i>	3.3 ± 0.2	4.1 ± 0.3	3.9 ± 0.2
3	<i>B.subtilis</i>	3.1 ± 0.3	3.2 ± 0.3	3.4 ± 0.3
4	<i>S.typhi</i>	4.4 ± 0.3	4.9 ± 0.4	3.1 ± 0.3
5	<i>E.coli</i>	0.4 ± 0.1	1.1 ± 0.1	0.6 ± 0.1
6	<i>S.aureus</i>	4.6 ± 0.4	5.1 ± 0.4	4.7 ± 0.4

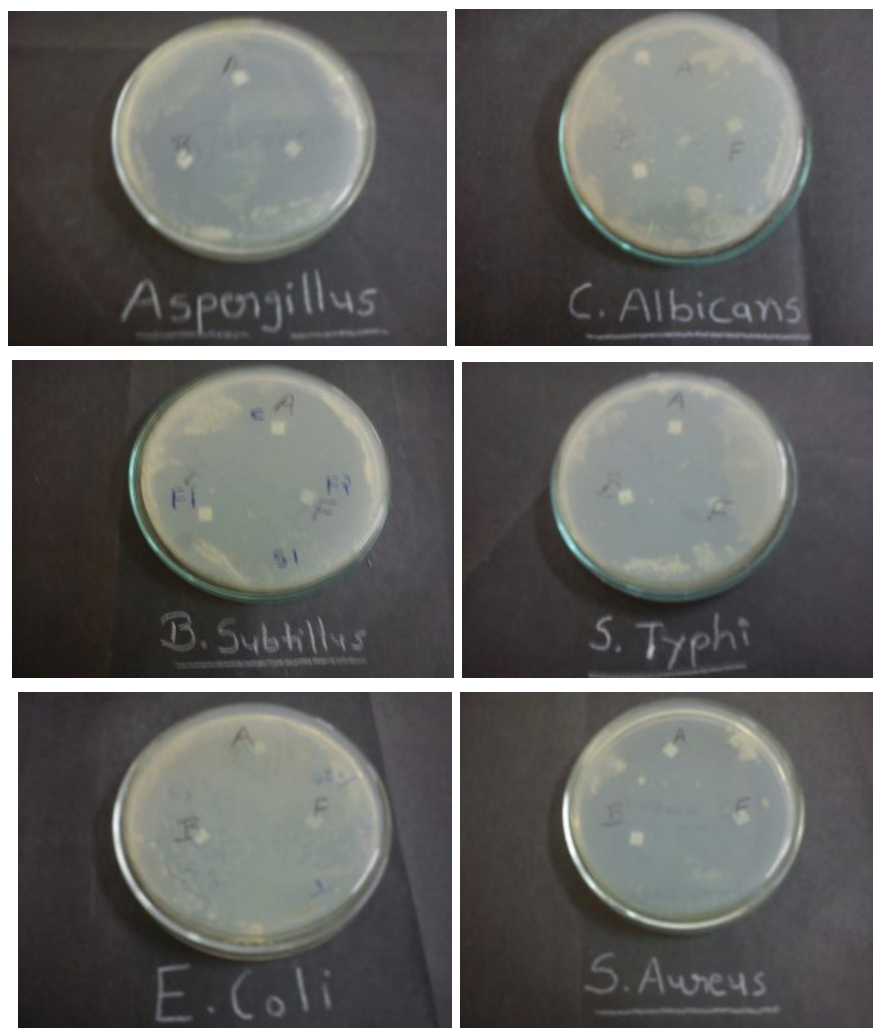


Fig. 3: Zone of inhibition against various micro-organisms

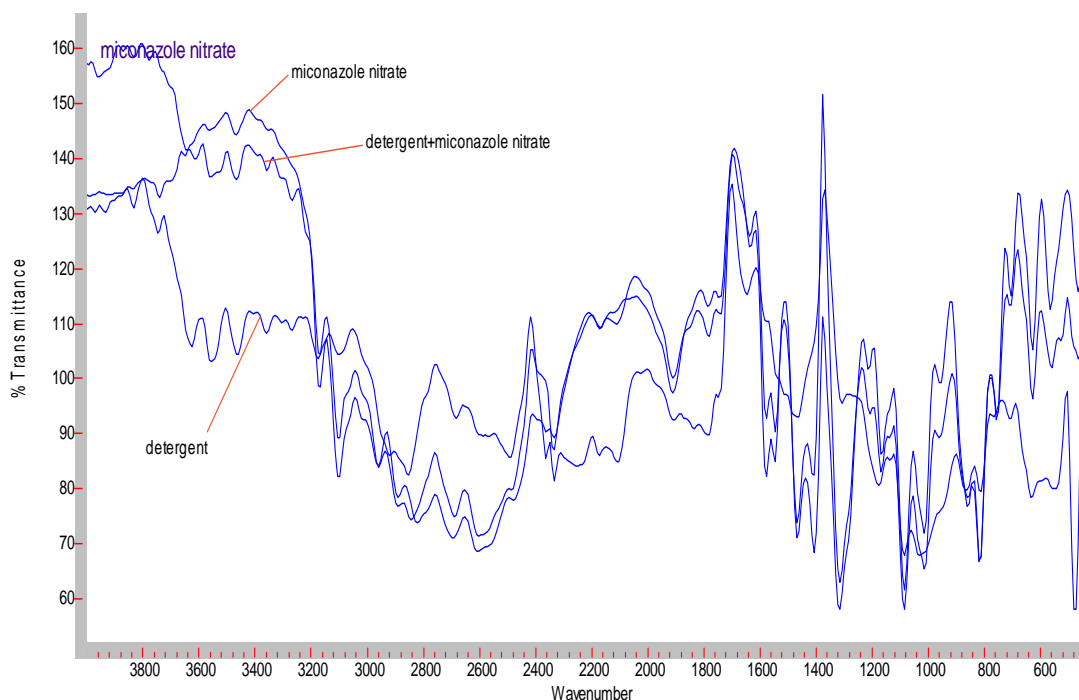


Fig. 4: IR spectral analysis for drug-excipient interaction

IR spectral analysis for drug-excipient interaction

The unsubstituted peaks in IR spectra indicate that there is no interaction between drug and soap.

CONCLUSION

From the prepared medicated soap strips, the strips of paper encoded B (Whatman filter paper no. 41) shows the best results as compared to other selected papers. The medicated soap strips show excellent release within 10 minutes indicating good efficiency and penetration. The prepared medicated soap strips are convenient to use and new type of dosage form for dermal infections such as candidiasis, aspergillus. It is useful for patients of all ages and sex.

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