



## Development and evaluation of medicated soap strip's of clotrimazole for dermal infection

Amit B. Patil<sup>\*1</sup>, Purushotham Rao K<sup>2</sup>, RN. Charyulu<sup>1</sup>, P. Prabhu<sup>1</sup>, Marina Koland<sup>1</sup>

<sup>1</sup>NGSM institute of pharmaceutical sciences, Paneer, Deralakatte, Mangalore, Karnataka, India

<sup>2</sup>H.K.E's college of pharmacy, Gulbarga, Karnataka, India

### ABSTRACT

The research is aimed to formulate clotrimazole paper soap strip that will result in faster drug release through foam; for better and effective relief from fungal infections like tinea, cutaneous candidiasis and seborrhoeic dermatitis. The formulation of medicated paper soap strips was carried out in two phases. Phase-I optimization Study, consist of formulation of non medicated paper soap strip; by randomly selecting marketed soap bars, then preparing their soap solution of varying concentration and then different pharmaceutical grade papers were dipped into these soap solution and air dried. The formulated soap strips were then evaluated for soap absorption capacity on paper, weight gain, thickness, size, shape, foam, and stability studies. From the results best soap, its soap solution concentration and paper was screened out. Phase-II study involves incorporation of drug into the best soap and its soap solution was achieved by emulsification technique and application of medicated soap solution over best paper was achieved by dipping technique. Medicated paper soap strip were characterized for thickness, weight, foam test, stability studies, drug content uniformity, FTIR, *in vitro* drug release studies carried out in 0.1N HCl media showed 40.17% drug release in 30 min. The primary skin irritation studies carried out on guinea pigs, showed no sensitization and edema on skin after 72 hours of application. Zone of inhibition has revealed the potential antimicrobial activity the drug formulation. The results of present study revealed that the prepared medicated paper soap strips of Clotrimazole is economic, convenient, gives good foam on application, uniform drug content and no skin irritation on animals.

**Keywords:** Clotrimazole; paper soap strip; foam.

### INTRODUCTION

Fungal infections are contagious and spreads easily just by close contact or sharing a comb or hairbrush with the infected person. They can be controlled in their initial stage by proper medications. For this purpose many topical drug delivery systems are available including medicated soap bars, shampoos etc; their disadvantages being their economy, wastage, recurrence of infection on reuse, no accurate dosage, less foam formation etc;. The stratum corneum is a rate limiting step that restricts the inward movement of drug (Elias MP, Grayson S. 1983). According to kinetics, the maximum rate of skin permission depends on the skin permeability coefficient and its equilibrium in the stratum corneum (Kydonieus AF, Berner Bret. 1987). The literature survey has revealed that in presence of thick foam the drug is absorbed twice faster in affected areas than in absence of foam (Rekacewicz I, *et al.* 1990). Hence present research work is designed to formulate a novel

drug delivery system in the form of medicated paper soap strip that will produce good foam on affected part, deliver the drug at faster rate, will be economic, convenient to use and effectively cure the topical fungal infection

### MATERIALS AND METHODS

#### Materials

Clotrimazole was a gift sample from Torrent Pharmaceutical Pvt. Ltd. Ahmadabad. Sabouraud's dextrose agar was a gift sample from HiMedia Laboratories Ltd., Mumbai. Soap Bar-A, Soap Bar-B and Soap Bar-C were purchased from local market. Whattmann filter paper No. 1, 40, 41 and 42 was a gift samples from Venkatesh Chemicals, Gulbarga. Butter Paper and Bond Paper (Royal Executive Bond) were purchased from local market. All the chemicals used in the study were of analytical grade.

#### Designing of clotrimazole paper soap strips

##### Phase-I studies: Optimization study

**a. Selection of soap solution:** Non-medicated soaps of three different brands were selected (purchased from local market) and coded as MB-A, MB-B and MB-C and liquid soap solution of varied concentrations (5, 10, 15% w/v) of each soap were prepared. The criterion to

\* Corresponding Author

Email: patilamit\_05@yahoo.co.in

Contact: +91-9738678943

Received on: 28-03-2011

Revised on: 02-06-2011

Accepted on: 08-06-2011

select a good soap was foam test (Indian Standard. 1996).

**b. Selection of paper:** Different branded pharmaceutical grade papers were selected in the present study and coded as A, B, C, D, E, F, G, H and I. The criteria for selection of a good paper being their absorption capacity, weight and thickness.

**c. Preparation of non-medicated paper soap strips:** All the soap bar were reduced to powder by grinding and further their soap solution of 5%, 10% and 15% w/v concentration were formulated. Selected pharmaceutical grade papers were dipped into the soap solution by using modified disintegration test apparatus and air dried for 12 h at room temperature. This technique is known as "Dipping Technique".

**d. Characterization of Prepared non-medicated paper soap strips:** The prepared formulations were subjected for the determination of size, shape, thickness, weight variation, pH and foam test as per the literature reported (Indian Standard. 1996) and an average result of 20 strips were considered.

#### Phase-II Studies: Formulation of medicated paper soap strips

**a. Incorporation of 1% clotrimazole in non-medicated soap strips:** The drug is incorporated in the selected formulation that yielded optimum good soap absorption capacity and foam test result from the report of phase-I studies.

Accurately weighted 1% w/v clotrimazole was mixed with soap powder and added to distilled water under constant and continuous stirring conditions until a uniform liquid soap-drug solution was formed. The medicated soap strips were prepared by "Dipping Technique" (Table 1).

**Table 1: Formulation of clotrimazole paper soap strips**

Sl. No	Composition	Quantity
1.	MB-C	15 g
2.	Clotrimazole	1 g
3.	Distilled Water Up to	100 mL

#### Size and shape

The size selected was 3 X 5 cm, rectangular shaped paper soap strip. The size and shape was randomly selected as it was convenient for dipping in a beaker and it was also similar to that of commercially available paper soap.

#### Weight gain test

Weight gain was calculated by using digital electronic balance. Subtracting the dry weight of the paper from the formulated paper soap strip represented the value for soap absorption capacity of the paper. An average of 20 non-medicated and medicated paper soap strips was considered.

#### Thickness test

The thickness of paper soap strip was calculated by using standard precalibrated Screw Gauge, by randomly measuring the thickness of the paper soap strip at five different parts and then calculating the mean average. An average of 20 non-medicated and medicated paper soap strips was considered.

#### In-vitro drug release studies under simulated dermatological conditions

The drug release from medicated soap strips was carried out by stationary dialysis method using prehydrated cellophane membrane as barrier in 0.1N HCl media which was maintained at 37 °C ±2 °C and 5 mL sample were withdrawn after every 5min up to 30 min. The drug content was estimated by measuring the absorbance at 263 nm in a 1700 UV Shimadzu Spectrophotometer (Prasad MT, Rambabu D, *et.al.*1993).

#### Primary skin irritation test

Skin irritation test three healthy guinea pigs of either sex were selected for the study and maintained with normal food and water during the test period of 72 h. The hair from the upper portion of waist (lower back portion) was shaved and cleaned with surgical spirit to expose sufficiently large test area. Thick foam, obtained on hydration of a soap strip in 2 mL of distilled water was applied to the test area of each animal. Animals were under observation for any erythema and / or edema for 72 h.

#### Microbiological studies

Sampling was done by collecting scrapings from the diseased patient under the supervision of Dermatologist using the standard cup plate method. The samples were stored in peptone water, before inoculation into sabouraud's dextrose agar media and then incubated at 30 °C for 5-7 days. Antifungal activity of prepared formulations were tested against the organism involved in superficial fungal infection such as *pityriasis versicolor* (*Tinea versicolor*) and seborrhoeic dermatitis by hydrating clotrimazole paper soap strips with 2 mL distilled water, then placing them in the cavity made in the agar media (Parise DM.1990).

#### Stability studies

The stability studies were performed at 37 °C ±2 °C over a period of six months on the prepared medicated paper soap strips. Changes in pH, physical appearance and drug content were estimated at different time intervals.

#### IR spectral analysis for drug-exciipient interactions

The drug-exciipient interactions study was carried out using IR spectroscopy method with the help of PerkinElmer 1615 spectrophotometer (Indian Pharmacopoeia. 1996).

**RESULTS AND DISCUSSION**

**Phase-I studies: Optimization study**

On evaluation and comparison of results from histogram, of all the formulated non-medicated paper soap strips; the paper coded F was found to have optimum soap absorption capacity with weight gain or the soap absorption capacity of 0.31g (Figure 1), thickness gain of 0.23mm (Figure 2) and showed no signs of cracking, flaking or peeling after drying. Foam test revealed that the formulation 'F' showed highest foam stability with foam height of 31 mL; when formulated in 15% w/v of soap solution of the soap coded MB-C (Figure 3). All the soap strips were having pH in the range of 7.00 to 7.2.

It was thus evident from the phase I study results that, 1% clotrimazole drug was to be incorporated in non-medicated paper soap strip formulated from the paper coded 'F' that was dipped in the 15% w/v soap solution

of soap MB-C.

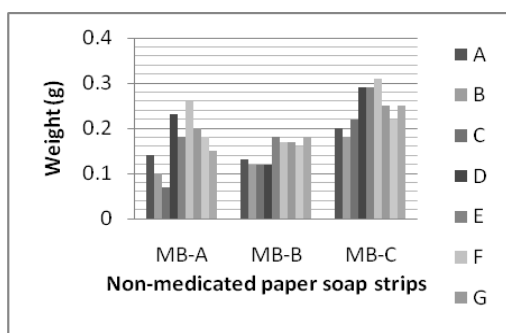
**Phase-II Studies: Formulation of medicated paper soap strips**

The formulated 1% Clotrimazole paper soap strips was found to have uniform drug content of 99.0%, with the weight gain of 0.47 g and 0.24 mm of thickness and an optimum foam stability and height of 49 mL. The *In-vitro* drug release showed 40.17% drug released from 1% clotrimazole paper soap strips at the end of 30 min (Table 2).

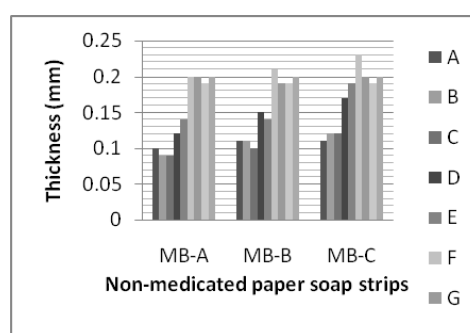
The primary skin irritation test revealed that none of the prepared clotrimazole paper soap strips showed any kind of erythema and / or edema, after 24 h, 48 h and 72 h of application, this indicated that the prepared formulations were non-irritant on the skin of guinea pig.

Microbiological study showed good zone of inhibition i.e., 1.16 cm. of diameter for 1% clotrimazole paper

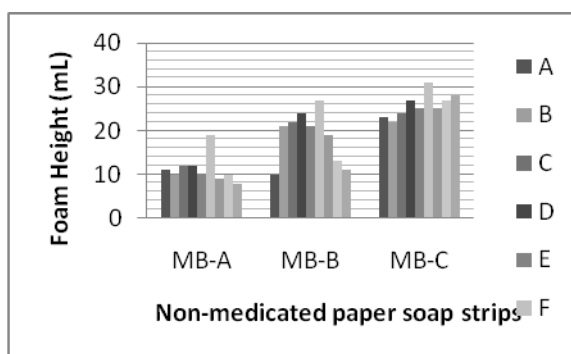
**Histogram showing optimization experimental results of non-medicated paper soap strips prepared from soap solution (15% w/v)**



**Figure 1: Thickness (mm)**



**Figure 2: Weight (g)**



**Figure 3: Foam Height (mL)**

**Table 2: In-vitro drug release profile of 1% clotrimazole paper soap strips**

Sl. No.	Time (min)	Square root of time (min)	Cumulative percent drug released	Cumulative percent drug retained	Log Cumulative percent drug retained
1.	0	0.000	0.00	0.00	0.000
2.	5	2.236	11.78	88.22	1.945
3.	10	3.162	16.78	83.22	1.920
4.	15	3.872	22.50	77.50	1.889
5.	20	4.472	28.75	71.25	1.852
6.	25	5.000	35.17	64.83	1.811
7.	30	5.477	40.17	59.83	1.776



Before Application

After 72 h of Application

**Figure 4: Primary skin irritation test of 1% clotrimazole paper soap strips**



1% clotrimazole paper soap strip



controlled sample of drug

**Figure 5: Microbiological Studies (Zone Of Inhibition)**

soap strip as compared to controlled sample of drug (Rekacewicz I, *et al.* 1990).

Stability study results proved no significant change in pH, physical appearance and drug content in the formulations and hence found to be stable. IR spectral analysis showed the undisturbed peaks of pure drug at  $1114.27\text{ cm}^{-1}$  which is due to C-N group and  $765.54\text{ cm}^{-1}$  due to C-Cl in the 1% Clotrimazole medicated paper soap strips; confirm that there is no drug excipient interaction in the prepared formulations.

#### CONCLUSION

The purpose to develop and evaluate a novel drug delivery system in the form of clotrimazole soap strips was achieved; as the results revealed that the medicated soap strips produced good foam on affected part, delivered the drug at faster rate, is economic, convenient and can effectively cure the topical fungal infection. The formulation is designed for the use to the patients of all ages and sex.

#### REFERENCES

Elias MP, Grayson S. The Stratum Corneum. 1<sup>st</sup> ed. New York: Springer-Verlag 1983; p.53-67.

Indian Pharmacopoeia, Controller of Publications, Ministry of Health and Family Welfare, Government of India, Delhi, 1996; S-23.

Indian Standard. Shampoo, Soap based-specification (first revision). IS 7669-1990: 1996; No-Annexa. B-2; p. 2-4.

Kydonieus AF, Berner Bret. Transdermal Delivery of Drugs. 3<sup>rd</sup> ed. Boca Raton: CRS Press Inc 1987; p.5-21.

Parise DM. Tinea versicolor a practical guide for primary care physician. J Postgrad med 1990 May; 1587(7): 61-2.

Prasad MT, Rambabu D, Apte SS, Venkateshwar Rao G, Sarveswar Rao VV, Ramesh Rao B. *In-vitro* release and Anti-fungal activity of commercial clotrimazole creams. Indian J Pharm Sci. 1993; 55(4): 119-23.

Rekacewicz I, Guillaume JC, Benkhrel F, Archimabaub A, Basperyras M, Biotier F, *et al.* A double-blind placebo-controlled study of 2% foaming lotion of ketoconazole in single application in the treatment of pityriasis versicolor. Ann J Dermatol Venereol. 1990; 117(10): 709-11.