INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Research Article……!!!

Received; accepted

DESIGN AND PRECLINICAL STUDIES OF MICONAZOLE SOAP STRIPS FOR DERMAL INFECTIONS

K.Purushotham Rao*[1],Thimothy Maitho[2], E.K.Kamamia[2], Amit.B.Patil[1], Prashant Sagre[3]

1. H.K.E.'s College of Pharmacy, Gulbarga (Karnataka)
2. Dept of Pharmacy,Mount Kenya University,Kenya.
3. M.R. Medical College & General Hospital, Gulbarga (Karnataka)

Keywords:
Miconazole, Medicated paper soap strips and foam

For Correspondence:

Dr.K.Purushotham Rao

H.K.E.'s College of Pharmacy, Gulbarga (Karnataka)
India

E-mail:
kprao369@rediffmail.com

ABSTRACT

Ringworm (tinea) is a fungal skin infection caused by several different fungi and generally classified by its location on the body. Despite its name, ringworm infection does not involve worms. The name arose because of the ring-shaped skin patches created It may be caused by *Trichophyton, Microsporum,* or *Epidermophyton.* The infection generally produces round patches with pink scaly borders and clear areas in the center. Sometimes the rash is itchy. Body ringworm can develop anywhere on the skin and can spread rapidly to other parts of the body or to other people with whom there is close bodily contact by the infection.Superficial fungal infections of the skin and mucous membrane respond readily to topical application of antifungal agents.. The preparation and study of medicated paper soap strips was carried out in two phases. In Phase-I Studies optimization was done for water absorption capacity of paper by determining weight gain, thickness, size & shape, foam test and stability studies. From these parameters soap concentration of liquid soap solution and paper is screened out. In Phase-II Studies optimized concentration of liquid soap solution and paper which were chosen for incorporation of drug and prepare medicated paper soap strips by emulsification technique and application of soap solution over paper was achieved by dipping technique and characterized for thickness, weight, foam test, stability studies, drug content uniformity, FTIR, in vitro drug release studies which were carried out in 7.4 PH media using prehydrated cellophane membrane for 30 mins. The results indicated that 48.28 % drug release in 30 mins. The primary skin irritation studies carried out on rabbits and guinea pigs showed no sensitization and edema on skin after 72 hours of application. The microbial studies indicated the drug action through zone of inhibition. The results of present study revealed that the prepared medicated paper soap strips of miconazole is economic, convenient, gives good foam on application without any skin irritation.

INTRODUCTION:

Fungal infections like tinea, cutaneous candidiasis and seborrhoeic dermatitis is always a worry and uneasiness to the suffering patients; hence the drug selected in the present study is miconazole which has broad spectrum antifungal activity and belongs to azole class. Presence of thick foam on the infected part causes hydration of stratum corneum for better permeation of drug.[1,2,3,4,5] Fungal infections are contagious, spread from person to person. Close contact or sharing a comb or hairbrush with someone who has tinea can spread the fungus from one person to another. Because fungi need a warm, dark, and humid place to grow, public showers, pools, locker rooms, and even the warmth of shoes and socks can give fungi the perfect opportunity to strike. They can be controlled in their initial stage by proper medications. For this purpose there are many topical drug delivery systems available including medicated soap bars and shampoos etc. Their disadvantages being their economy, wastage, recurrence on reuse, no accurate dosage, formation of foam etc. hence the present work is designed to formulate and evaluate medicated soap strips to counter all the above disadvantages.

MATERIALS AND METHODS:

Miconazole was gift sample from Torrent Pvt. Ltd. Ahemadabad. Sabouraud's dextrose agar was a gift sample from Himedia Laboratories Ltd., Mumbai. Soap Bar-A Soap Bar-B Soap Bar-C were purchase from Local Market. Whattman filter paper No. 1, 40, 41 & 42 was a gift sample from Venkatesh Chemicals, Gulbarga. Butter Paper and Bond Paper (Royal Executive Bond) were purchase from Local Market. HCL was purchased from Qualigen Fine Chemicals, Mumbai.

Preparation of formulation: Phase-I Studies: Optimization Experiments.

Selection of Soap Solution: Three non-medicated soaps of different brands were selected and coded as MB-A, MB-B and MB-C and liquid soap solution of varied concentrations (5, 10, 15% w/v) were prepared. During the preparation of Liquid soap solutions formation of bubbles and lumps was avoided. The criteria to select a good soap was foam test.

Selection of paper: Nine different branded papers 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.

Preparation of non-medicated paper Soap Strips: The paper Soap Strips was prepared by "Dipping Technique" using modified disintegration apparatus and air dried for 12 hours at 37±2°C.

Characterization of Prepared soap strips: The prepared formulations were subjected for the determination of size and shape, thickness, weight variation, pH and Foam tests by reported standard methods and an average result of 20 strips were taken.

Phase-II Studies:Formulation of Medicated Paper Soap Strips: The drug is incorporated in the selected formulation which yielded good soap absorption capacity in phase-I studies. Accurately weighted drug 2% Miconazole mixed with soap powder and added to distilled water under constant and continuous stirring conditions for 1 hour. Until a uniform liquid soap-drug solution was formed and then the paper soap strips were prepared (Table-1).

***In-vitro* drug release studies under simulated dermatological conditions:**[6,7,8] The drug release from medicated Soap Strips was carried out by stationary dialysis method using prehydrated cellophane membrane as barrier in 7.4 PH media which was maintained at 37°C temperature for a period of 30 minutes. 10ml. samples were collected from the receptor compartment and the same ml. of fresh 7.4 PH was replaced at every 10 minutes time interval for a period of 30 mins. The drug content was estimated by measuring the absorbance at 226.2 nm in a 1700 UV Shimadzu spectrophotometer.

Primary Skin Irritation Test:[9] 3 healthy rabbits and guinea pigs of either sex were selected for the study and maintained with normal food and water during the test period of 72 hrs. The hair from the upper portion of waist (lower back portion) was shaved and cleaned with surgical spirit to expose sufficiently large test area. A thick foam was 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 hours.

Microbiological Studies:[11,12,13] By taking scrapings collected 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 than incubated at 30°C for 5-7 days. Antifungal activity of prepared formulations were tested against lipophisic yeast Malassezia furfur (i.e., pityrosporum orbiculare and pityrosporum ovale) as the organism is involved with superficial infection such as pityriasis versicolor (Tinea versicolor) and seborrhoeic dermatitis.

Stability studies:[14] The stability studies were performed at 37°C ±2°C temperature over a period of six months on the prepared medicated paper soap strips pH the changes physical appearance and drug content was observed.

IR spectral analysis for Drug-excipient interactions:[15] The studies were carried out using IR method with the help of perkin-elmer 1615 spectrophotometer.

RESULTS AND DISCUSSION:

Among the several brands of water absorbable papers studied, the paper coded F was found to have optimum absorption capacity of soap with 0.21mm Thickness (Fig.No.1) & 0.30gm weight (Fig.No.2). Among the different brands of soaps in their varied concentrations studied; the formulation code F of 15% w/v liquid soap solution of soap MB-C yielded satisfactory foam test of 20ml foam height (Fig.No.3). All the Soap Strips have pH range of 7.00 to 7.1. The prepared 2% Miconazole formulations found to have uniform drug content 98.85%, weight of 0.50 gm. and 0.22mm of thickness. The medicated soap strips found to give optimum foam height of 49 ml. (Table No.-2) ***In-vitro*** **drug release** revealed that at the end of 30 mins. the % amount of drug released from 2% Miconazole paper Soap Strips was 48.28%. (Table-3). **Primary Skin Irritation Test** showed none of the prepared medicated paper Soap Strips showed any kind of erythema and / or edema, 24 hrs., 48 hrs. & 72 hrs. of application, indicating that the prepared formulations were non-irritant on the skin of rabbit and guinea pig. Microbiological Studies showed good zone of inhibition i.e., 1.19 cm. of diameter. **Stability studies** results revealed no change in pH and physical appearance and drug content in the formulations. **IR spectral analysis for Drug-excipient interactions:** the undisturbed peaks of pure drug at 1638.37 cm^{-1} which is due to carboxyl group and 1149.06 cm^{-1} and 1232.73 cm^{-1} due to alkyl aryl ethers in the 2% Miconazole medicated paper soap strips; confirms that there is no drug excipient interaction in the prepared formulations.

CONCLUSION:

The results of our study is economical, convenient to handle, carry and it is a new design of a dosage form to use for dermatological disorders of all age grouped patients.This is a industry based project further work is in progress.

Acknowledgement:

We express our thanks to Sri Simon Gicharu , Chairman, Mount Kenya University, Kenya for sponsoring this project and encouraging throughout the work period. The authors are also thankful to Principal of H.K.E.'s College of Pharmacy, Gulbarga for providing necessary laboratory facilities to carryout this work with great ease and precision and also thanks to Sipra Labs, Hyderabad for providing facilities of IR spectral analysis.

References:

1. Feldman, S.R., Sanghav, N., Setaluri, V., "Topical Corticosteroid in foam Vehicle offers comparable coverage compared with traditional vehicle", J. Am. Acad. Dermatol., 2000 Jan.; 42(6): 1017-20pp.
2. [No Author Listed], "Ketoconazole Foam – Connetics: Connetics Ketoconazole foam". Drug R.C., 2003, 4 (5): 323-5pp.
3. Misra, A.N., "The Skin", "Transdermal Drug Delivery System" in Controlled and Novel Drug Delivery by N.K. Jain. C.B.S. Publishers and Distributors. New Delhi; 1996, 101-103pp.
4. Montagna W., "The structure and function of skin", 3rd Edn., Academic Press, New York, 1974, 10 pp.
5. Indian Standard "Shampoo, Soap based-specification" (first revision). IS 7669-1990: 1996; No-Annexa B-2; 2-4pp.
6. Green C.A., Farr P.M. Shuster S. "Treatment of Seborrhoeic dermatitis of the face, scalp and trunk to topical ketoconazole; Response of seborrhoeic dermatitis of the face, scalp and trunk to topical ketoconazole". Briths Journal of Dermatology. 1987 July: 217-221pp.
7. Marry M., Carry, Pryce D.M. "Treatment of seborrhoeic dermatitis with ketoconazole: Response of seborrhoeic dermatitis of scalp to topical ketoconazole". British Journal of Dematology. 1987 July: 213-216pp.
8. Farr P.M., Shuster S. "Treatment of Seborrhoeic dermatitis with topical ketoconazole". Lancet 1984 Dec: 1271-1272pp.
9. Chamberlain, A.N.,Halablab, M.A., Gould, D.J. and Miles R.J. "Distribution of Bacteria on hands and the effectiveness of brief and through decontamination procedures using non-medicated soap". Zentralbi Bakteriol; 1997 April; 285(4): 565-75pp.
10. Tajima M. "Malassezia species in patients with seborrhoeic dematitis and atopic dermatitis". American Journal of Hospital Pharmacy. 1983: Vol. 40, Issue 8: 1334-1336 pp.
11. Lange D.S., Rechards H.M., Guarnieri J., Humeniuk J.M., Savin R.C. and Reyes B.A. et. al., "Ketoconazole 2% shampoo in the treatment of tinea versicolor: a multicenter, randomized, double-blind, placebo-controlled trial". J. Am. Acad. Dermatol. 1998 Dec: 39(6): 944-950 pp.
12. Indian Pharmacopoeia Government of India Ministry of Health and Family Welfare. Published by the Controller Publications. Delhi; 1996, 100pp.
13. British Pharmacopoeia published on the recommendation of Medicine Commission 1993: II: A-192pp.
14. Sethi P.D. "Quantitative Analysis of Drugs in Pharmaceutical Formulations", CBS Publishers and Distributors, Delhi, 2nd Edn., 1993: 466pp.
15. Indian Pharmacopoeia Government of India Ministry of Health and Family Welfare. Published by the Controller Publications. Delhi; 1996: S-51pp.

Phase-I Studies:

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

Fig. No.1: Thickness (mm)

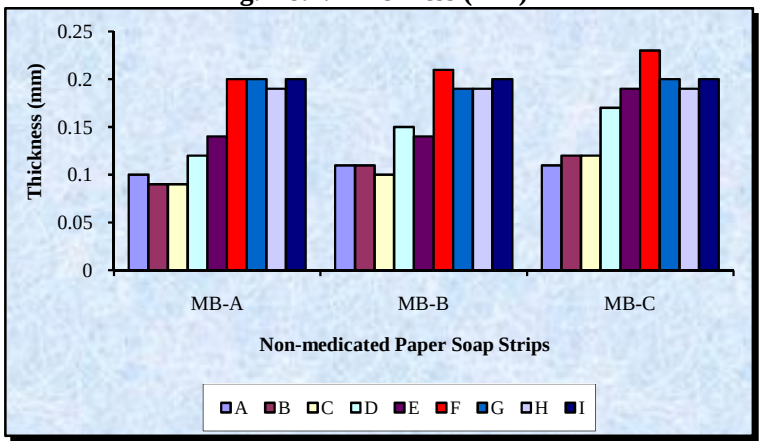

Fig. No. 2: Weight (gm)

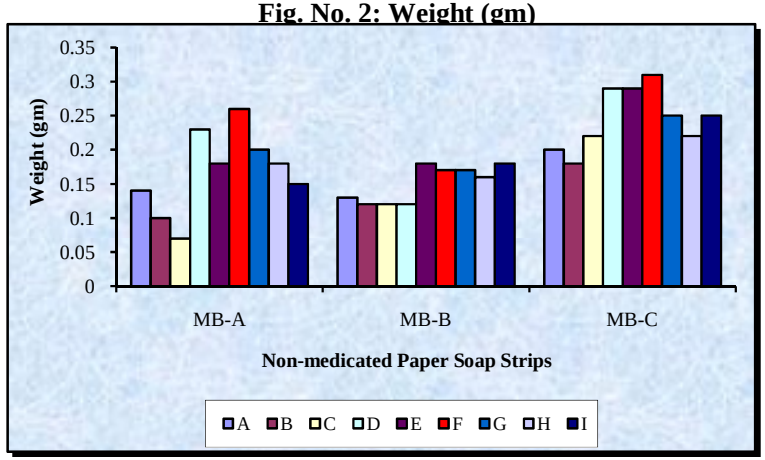

Fig. No. 3: Foam Height (ml.)

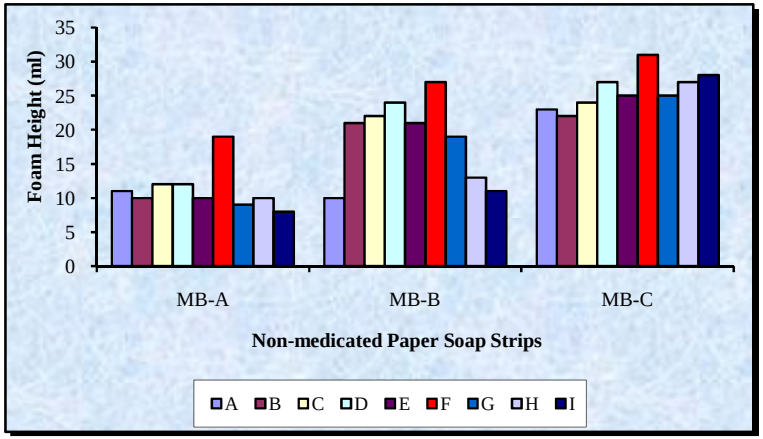

Table No. 1

Formula used to prepare Miconazole Paper Soap Strips

Sl. No	Ingredient	Quantity Taken
1.	MB-C	15 gms. Each
2.	Miconazole	2 gms.
3.	Distilled Water	100 ml.

Table No. 2

Physico-chemical Parameters of prepared Miconazole soap strips

Sl. No.	Parameters	2%Ketoconazole soap strips
1.	Thickness (mm)	0.21±0.02
2.	Weight variation (gm)	0.50±0.01
3.	Foam height (ml)	49±0.00
4.	Drug content (mg)	98.85%
5.	PH	7.0

Table No. 3

In-vitro drug release profile of 2% Miconazole Paper Soap Strips

Sl. No.	Time (mins)	Square root of time (mins)	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	18.42	81.58	1.937
3.	10	3.162	21.67	78.33	1.903
4.	15	3.872	28.32	71.68	1.878
5.	20	4.472	32.46	67.54	1.856
6.	25	5.000	38.21	61.79	1.801
7.	30	5.477	49.39	50.61	1.778

* Each reading is a mean of three replicates.

FIG-4: PRIMARY SKIN IRRITATION TEST OF

2% MICONAZOLE PAPER SOAP STRIPS

Before Application

After 72 hrs. of Application

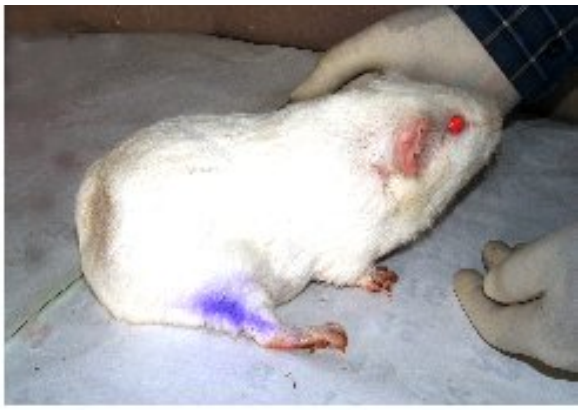

FIG-5: 2% MICONAZOLE PAPER SOAP STRIPS