In Vitro Antifungal Activity of Naftifine: (SN 105-843 GEL) Against Dermatophytes

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Abstract

Antifungal activity of naftifinc (SN 105-843 gel) a napthyle alkyleamine derivative, was measured in vitro against freshly isolated cultures of dermatophytie fungi. Using appropriate concentrations of naftifine, its antifungal activity was compared with the same concentrations of griseofulvin against Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton violaceum, Trichophyton tonsurans, Microsporum Canis and Epidermophyton floccosum.
The results indicated that minimal inhibitory concentration (MIC) for naftifinc was 0.1 Ug/ml against Trichophyton rub-rum, Trichophyton violaceum and Trichophyton tonsurans, whereas for griseofulvin the MIC was 0.5 UG/ml. This showed that naftifinc was more effective in vitro than griseofulvin against these fungi. The MIC of naftifinc and griseofulvin was identical i.e. 0.1 Ug/ml against Trichophyton mentagrophytes, Microsporum canis and Epidermophyton floccosum. (JPMA 31:279, 1981).

Introduction

At present the world is passing through an era of antibiotics, hormones and many other potent drugs. In recent years a number of synthetic and semi-synthetic compounds have been included in the list of effective drugs against fungal infections. (D. Arey and Scott, 1978; Maxwell and Bsady, 1971; Walker et al., 1978).
The current therapy of dermatomycoses now depends mainly on anti-fungal agents belonging to four different chemical groups, the imidazole, thiocarbaretes and antibiotics such as the polyenes and griseofulvin (D. Arcy and Scott, 1978; Elimin et al 1981). The present work deals with in vitro anti-fungal activity of naftifine (SN 105-843 gel), an alkylamine derivative, against freshly isolated cultures of dermatophytes. Chemically this compound is known as (E)-N-Methyle-N-(l-Nap-thyl)-3-phenyl-2-propen-l-amine hydrochloride.
This was a trial drug synthesised and supplied by Sandoz Ltd., Switzerland. The research work was carried out in collaboration with the Dermatology Department of Jinnah Postgraduate Medical Centre, Karachi and Department of Microbiology, University of Karachi.

Material and Methods

This research work was divided into two phases. The first phase dealt with the isolation of dermatophytes from different types of clinical material and their identification -and the second phase with antifungal activity of naftifine.
Phase I
Stock-cultures maintained in the laboratory may lose their pathogenicity by repeated subcultures. To avoid this, freshly isolated cultures from one hundred patients suffering from various types of dermatomycoses were used in this study. These patients were seen at the Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi. The material from skin, hair and nails was collected after cleaning with 70% methylated alcohol. Part of it was examined in 10% KOH and part cultured on

mycobiotic agar (Difco Supplementary Literature, 1962;. All patients with clinical diagnosis of fungus infection were confirmed by microscopic demonstration of the myecilial filaments in clinical material followed by the isolation and identification of the cultures.

Phase II

The isolated dermatophytes were grown on Sabouraud's dextrose agar and were identified on the basis of gross morphological characteristics, microscopy, pigment productions and physiological characteristics (Table I).

Table I

Positive Results—Clinically, Microscopically and Culturally

	Clinically	*Micro-scopically*	*Culturally*	*Negative both Microsco-pically & culturally*	*Total Cases*
Tinea corporis	37	33	33	4	37
Tinea capitis	34	27	27	7	34
Tinea cruris	26	18	18	8	26
Tinea pedis	01	01	01	Nil	01
Tinea barbae	02	02	02	Nil	02

In Vitro Testing

Sabouraud's dextrose slants of naftifine and griseofulvin were prepared in concentration of 2 Ug/ml, 1 Ug/ml, 0.5 Ug/ml, 0.1 Ug/ml, 0.05 Ug/ml and 0.01 Ug/ml by serial dilution method. Slants of each concentration in triplicate of both naftifine and griseofulvin were inoculated and incubated at 29°C for 7 days. Three slants devoid of these two drugs were also treated with the same amount of inoculum, which served as positive control.

Table II

Types of Dermatophytes Isolate from Various Cases

	Tricho-phyton rubrum	*Tricho-phyton violaceum*	*Tricho-phyton tonsurans*	*Tricho-phyton mentagro-phytes*	*Epiderm.o-phyton floccosum*	*Micros-porum Canis*	*Total*
Tinea corporis	28	03	Nil	02	Nil	Nil	33
Tinea capitis	01	23	02	Nil	Nil	01	27
Tinea cruris	16	01	Nil	Nil	01	Nil	18
Tinea pedis	01	Nil	Nil	Nil	Nil	Nil	01
Tinea barbae	02	Nil	Nil	Nil	Nil	Nil	02
							81

The minimal inhibitory concentration was determined by serial dilution. The presence or absence of growth in each triplicate concentration of naftifine and griseofulvin was compared with each other and also with the positive control containing no drug (Table III).

TABLE III

COMPARATIVE INHIBITORY EFFECT IN VITRO OF NAFTIFINE AND GRISEOFULVIN AGAINST ISOLATED DERMATOPHYTES

DERMATOPHYTES	NO.OF ISOLATES TESTED	DAYS OF INCU-BATION	DILUTION IN UG/ML NAFTIFINE 2	1	0.5	0.1	0.05	0.02	CONTROL	GRISEOFULVIN 2	1	0.5	0.1	0.05	0.01	CONTROL
TRICHOPHYTON RUBRUM	48	7 DAYS	-	-	-	-	++++	++++	++++	-	-	-	++	++++	++++	++++
TRICHOPHYTON VIOLACEUM	27	7 DAYS	-	-	-	-	++	++++	++++	-	-	-	++	++++	++++	++++
TRICHOPHYTON TONSURANS	02	7 DAYS	-	-	-	-	++	++++	++++	-	-	-	++	++++	++++	++++
TRICHOPHYTON MENTAGROPHYTES	02	7 DAYS	-	-	-	-	+	++	++++	-	-	-	-	++++	++++	++++
MICROSPORUM CANIS	01	7 DAYS	-	-	-	-	+++	+++	++++	-	-	-	-	+++	+++	++++
EPIDERMOPHYTON FLOCCOSUM	01	7 DAYS	-	-	-	-	++++	++++	++++	-	-	-	-	++++	++++	++++

KEY

- COMPLETE INHIBITION
+ FAIR GROWTH
++ MODERATE GROWTH
+++ GOOD GROWTH
++++ MAXIMUM GROWTH

Results

The MIC of naftifine was determined in comparison with griseofulvin in vitro against eighty one isolates of dermatophytes, which included Trichophyton rubrum (forty-eight isolates), Trichophyton violaceum (twenty-seven isolates), Trichophyton mentagrophytes (two isolates), Trichophyton tonsurans (one isolate), Microsporum canis (one isolate) and Epidermophyton floccosum (one isolate)

(Table II). These cultures were isolated from patients suffering from dermatophytoses (Table I). Naftifine has shown interesting inhibitory effect on these fungi. It inhibited the growth of Trichophyton tonsurans, Trichophyton ruhrum and Trichophyton violaceum in concentration of 0.1 Ug/ml, whereas griseofulvin in this concentration did not inhibit the growth (Table III). The MIC of naftifine and griseofulvin is therefore 0.1 Ug/ml and 0.5 Ug/ml respectively (Roth at al, 1959).
Equal inhibitory effect of both of these drugs was obtained against Trichophyton mentagrophytes, Epidermophyton floccosum and Microsporum canis. The MIC against these fungi was 0.1 Ug/ml.

Discussion

Naftifine is a napthyle alkylamine derivative, a class of compounds that has never been used in chemotheraphy. The aim of the investigation was to determine the spectrum of activity against various species of dermatophyte fungi in vitro in comparison with griseofulvin.
The increased incidence of fungal infection and non-availability of effective drugs has stimulated vigorous search for antifungal anti-biotics (D. Arcy and Scott, 1978; Maxwell and Brady, 1971; Walker et al., 1978; Kurnatowska and Kwasniewska, 1978; Elimin et al., 1981).
From the in vitro results achieved with eighty one fresh clinical isolates of dermatophytes which included six species-Trichophyton (four), Microsporum (one) and Epidermophyton (one), it can be seen that naftifine is highly active against certain dermatophytes (Table III). Its degree of efficacy is markedly superior to that of griseofulvin in vitro (Brian, 1949; Genltes, 1966). Its spectrum of activity in vitro has justified an investigation of this compound in vivo. The authors have conducted a study which confirms its efficacy in vivo also (Haroon et al., 1981).
Results in vitro indicated that MIC of naftifine and griseofulvin was 0.1 Ug/ml and 0.5 Ug/ml respectively against Trichophyton rubrum, Trichophyton violaceum and Trichophyton tonsurans (Table III). Roth, Salman and Blank in 1959 while studying sensitivity of dermatophytes to griseofulvin found that MIC of this antibiotic to be as low as 0.14 to 0.44 Ug/ml. Our results are also in agreement with these findings. This trial drug as compared to griseofulvin was more effective against Trichophyton rubrum, Trichophyton violaceum and Trichophyton tonsurans. However the MIC of both naftifine and griseofulvin was almost equal i.e. 0.1 Ug/ml for Trichophyton mentagrophytes, Mocrosporum canis and Epidermophyton floccosum. It was found to be fungicidal.

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