

# THE EFFECT OF TOPICAL RETINOIC ACID (AIROL) IN THE TREATMENT OF TINEA VERSICOLOR

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## INTRODUCTION

Among the various kinds of superficial dermatomycosis, tinea versicolor is known as very resistant to treatment and has a very high prevalence in tropical countries like Indonesia. Several topical preparations have been used to cure this disease but the results were unsatisfactory, especially in cases showing large lesions.

The beneficial effect of selenium sulfide in the treatment of tinea versicolor was reported by Tinthoin in 1967 but the difficult method of application and the relatively long period of treatment may lead to irregular administration, thus increasing the chances of failure. Besides, the prolonged use of selenium on a large area of the skin may cause toxic reactions and extend the period needed to normalise the pigmentation of the affected skin. Recent studies on the treatment of tinea versicolor using locally applied preparations have confirmed the efficacy of miconazole nitrate (Achten *et al.*, 1971; Bamford, 1974; Budimulja *et al.*, 1974).

However, our experience (unpublished data) with miconazole nitrate in tinea versicolor showed that this drug gave less satisfactory results than in other kinds of dermatomycosis. This was mainly based on the high frequency of relapse and the long duration of treatment. Moreover, the time for the affected skin to regain normal pigmentation seemed to be quite extended. It is common knowledge that topical retinoic acid is widely used with satisfactory results for the treatment of

various degrees of acne vulgaris (Handojo and Susilorini, 1973; Handojo, 1977).

In our study on retinoic acid in the treatment of acne vulgaris (Handojo and Susilorini 1973), especially when located on the back and accompanied by macules of tinea versicolor in the surrounding area, the application of retinoic acid on the whole of the back gave marked improvement and total healing of the macular patches of tinea versicolor.

This finding with retinoic acid, the method of application and good tolerance by the patients, led to the conducting of a clinical study on the efficacy of retinoic acid applied topically in the treatment of tinea versicolor.

## MATERIALS AND METHODS

This clinical trial was carried out with 50 ambulatory patients (aged 8-56 years, 27 males and 23 females) attending the private practice of one of the authors and suffering from tinea versicolor of various degrees of severity. Previously, treatment had failed in 34 patients using the following anti-fungal drugs:

- (i) miconazole nitrate for 4-6 weeks in 2 patients;
- (ii) salicylic acid 10% in alcoholic lotion for 1-2 months in 17 patients;
- (iii) resorcine 3% plus sulfur praecipitatum 10% in alcoholic lotion or ointment for 4-6 weeks in 6 patients;
- (iv) salicylic acid 4%, benzoic acid 4% and iodine 0.5% in alcoholic lotion for 3-4 weeks in 9 patients.

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In this trial two types of topical retinoic acid (Ainol) were used, namely: Retinoic acid 0.05% in vanishing cream; and retinoic acid 0.05% in equal parts of propylene glycol and 95% alcohol.

The patients were entered at random in this trial and divided into the two groups: 25 patients received Ainol cream 0.05% applied twice daily and 25 patients received Ainol lotion 0.05% applied twice daily.

Following withdrawal of previous treatment, topical Ainol was applied on all visible macules of tinea versicolor. Each week clinico-morphological, microscopic and Wood's light examinations were carried out.

Diagnosis was made clinico-morphologically and confirmed by microscopic examination of the skin scrapings. A mixture of 9 parts of potassium hydroxyde 20% and one part of Parker super-chrome blue-black ink was used to stain the skin scrapings. Wood's light was used to locate all areas of infection.

Treatment was discontinued if Wood's light and microscopic examination of all visible macules of tinea versicolor gave a negative result, or after 3 weeks treatment Wood's light and/or microscopic examination still gave a positive result.

The efficacy of the preparations used was evaluated as follows: (i) Cured: if all visible macules/ex-macules showed a negative result with Wood's light and microscopic examination. (ii) Uncured: if after 3 weeks treatment some or all macules still showed a positive result with Wood's light and/or microscopic examination.

The final evaluation was done one month after cessation of treatment to detect relapses proved by a positive result on examination of the ex-macules with Wood's light and/or microscopic study.

## RESULTS

Out of the 50 patients entered in this study, 4 failed to complete the treatment and were thus lost for evaluation. It was not practical to make home visits or follow up absconders.

The number of patients followed up until the end of the treatment period could be specified as follows:

- (i) 23 patients (92%) in the group receiving Ainol cream 0.05%.
- (ii) 23 patients (92%) in the group receiving Ainol lotion 0.05%.

Table 1

Results of treatment with topical Ainol during 2 to 3 weeks in two groups of patients suffering from tinea versicolor.

Type of Ainol	Results				Relapses	
	Cured		Uncured		No. of patients	Per cent
	No. of patients	Per cent	No. of patients	Per cent		
Cream 0.05%	22	95.65	1	4.35	1	4.35
Lotion 0.05%	23	100.00	0	0	1	4.35
Total	45	97.83	1	2.17	2	4.35

Table 2

Period needed to cure tinea versicolor with topical AiroL.

Type of AiroL	Period to cure			
	2 weeks		3 weeks	
	No. of patients	Per cent	No. of patients	Per cent
Cream 0.05%	16	72.73	22	95.65
Lotion 0.05%	17	73.91	23	100.00
Total	33	73.33	45	97.83

The results of treatment in the 46 patients followed up until the end of the trial are summarized in Table 1.

Table 1 shows one patient (2.17%) in the group treated with AiroL cream 0.05% as uncured; some of his lesions still showed a positive result with the microscopic and Wood's light examinations.

No failures were found in the group of patients treated with AiroL lotion 0.05%. However, the difference in the cure rate between these two groups is statistically insignificant.

The treatment period needed to obtain a favourable result was relatively very short, namely: 2 weeks in 33 patients (73.33%) and 3 weeks in 45 patients (97.83%) with a mean of 2.27 weeks (see Table 2).

On average, the colour of the affected skin returned to normal within 2-4 weeks (Figs. 1 & 2). Further, lesions located on exposed parts of the skin returned to normal pigmentation more quickly than ones located on covered parts of the skin. Two relapses, one treated with AiroL lotion for two weeks and the other with AiroL cream for the same period, were found one month after cessation of treatment.

Moderate to severe desquamation was observed in almost all patients (97.82%), while mostly slight to moderate erythema was

seen in only 36.96% of the patients treated. It is worth mentioning that these irritant side reactions were more pronounced on the affected skin than on the normal one. Allergic reactions, local as well as systemic, were not encountered in this study.

#### DISCUSSION

The criteria for a successful treatment of tinea versicolor using locally applied preparations are generally based upon the following:

- (i) A high cure rate and a low relapse rate, as confirmed by the absence of the causative agent.
- (ii) Good tolerance judged by the low incidence of hypersensitive reaction and an acceptable local irritating effect.
- (iii) A "restitutio ad integrum", is a crucial factor, especially from a cosmetic point of view.

As with salicylic acid and resorcine (keratolytics), AiroL has a potent peeling action on the skin, thereby causing some desquamation and thinning effect on the horny layer, thus becoming unfavourable for the growth of dermatophytes.

It goes without saying that retinoic acid is a potent agent for use in dermatomycosis, especially tinea versicolor, and beyond any doubt its peeling effect plays a distinct role in the action of this preparation. However, in

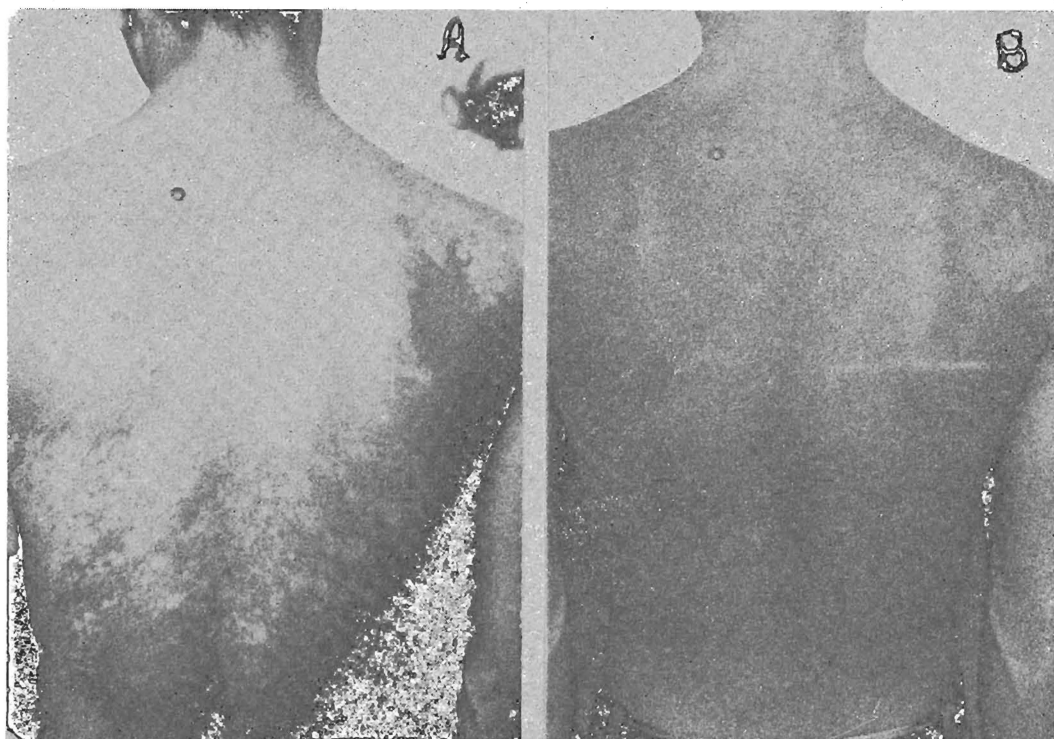


Fig. 1—Large hypopigmented lesions of tinea versicolor in a 30-year-old male subject. a) before treatment b) 4 weeks after treatment was started or 2 weeks after its cessation.

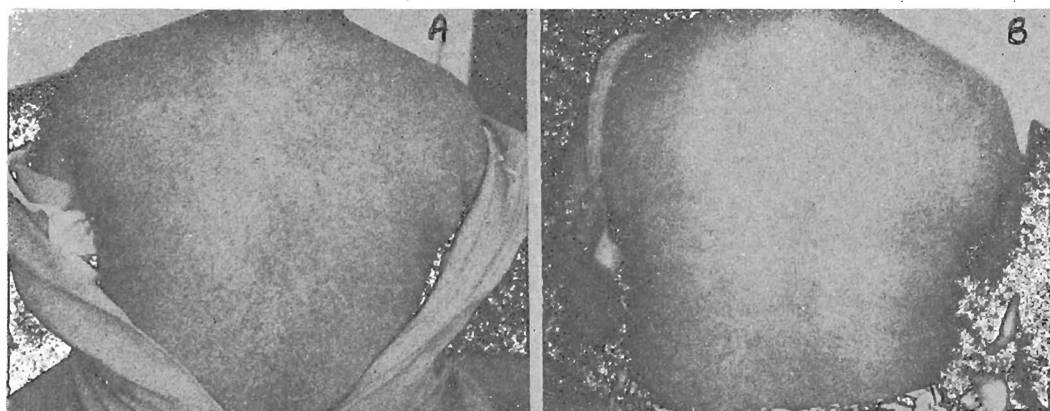


Fig. 2—Tinea versicolor in a 20-year-old female subject. a) before treatment b) 3 weeks after treatment was started or one week after its cessation.

spite of similar peeling activity, these agents have different degrees of efficacy on dermatophytes. In this regard, Airol can be said to be markedly superior to salicylic acid and resorcinol.

In an experimental study on the growth of dermatophytes in Sabouraud's glucose agar medium (pH adjusted to 5.4 - 5.6) we found (to be published) that by adding retinoic acid in a concentration of 0.015%, the growth of

dermatophytes (*Trichophyton*, *Epidermophyton* and *Microsporum*) was totally inhibited, as well as the growth of contaminants. On the other hand, a concentration of 0.01% only partially inhibited the growth of the dermatophytes mentioned above.

The results of this study show that *in vitro* retinoic acid has an anti-fungal action and it is clear that this occurs *in vivo* as well, as proved in this trial by the absence of the causative agent on microscopic examination and by the low incidence of relapse.

Another important feature of retinoic acid is its deep penetrative capacity which makes it possible to reach the deeply seated *Malassezia furfur*—the aetiological agent of tinea versicolor—and destroy it. As far as is known, this deep penetrative capacity of retinoic acid is not found in any other anti-fungal preparation.

Annoying local irritant effects which cause patients to abandon treatment were not encountered in our study. Instead, desquamation which occurred in almost all patients was accepted as a sign of healing, while the mostly slight or moderate erythema in 36.96% of the cases did not cause any subjective trouble.

Besides, neither systemic nor local allergic reactions were found in our series of patients. Thus, the good tolerance and acceptable degree of local irritation make Airol a suitable drug for use in tinea versicolour.

It must be remembered that hypopigmentation due to tinea versicolour is another problem to be considered as the disappearance of this symptom determines also the final outcome of treatment.

Although other anti-fungal preparations like miconazole nitrate, bis-phenyl-1-imidazolyl-methane and selenium sulfide are known to rapidly suppress the growth of *Malassezia furfur*, hypopigmentation of the affected skin

persists many weeks after treatment. From a cosmetic point of view, this gives the patients the impression of a therapeutic failure. But with retinoic acid, repigmentation of the affected skin occurs in an obviously shorter period especially when exposed simultaneously to sunlight. Accompanying peeling, an increase in quantity and enzymatic activity of dopa-positive melanocytes are found which ensures a quicker repigmentation of the lesions treated (Mills and Kligman, 1974).

It is why the use of topical retinoic acid is preferable when the lesions are hypopigmented. It is well worth noting that hypopigmentation due to tinea versicolor is commonly found in patients with a dark skin.

However, it has to be remembered that hyperpigmented macules may also be found in tinea versicolor; in that case exposure of the affected skin to sunlight has to be avoided.

Compared with the results obtained by Budimulja *et al.*, (1975) in a study using miconazole nitrate for the treatment of tinea versicolor (cure rate 92% and drop-out rate 50%), the results of our study showed a higher cure rate (97.83%) and a significantly lower drop-out rate (4%). Besides, much less time was needed to eliminate the pathogenic fungus (average 2.27 weeks) with a much lower relapse rate (4.35%).

The one failure with topical Airol, previously successfully treated with miconazole nitrate for one month, was due to a lack of regular and thorough drug application.

As was enunciated by Knudsen (1975) the hyphae of dermatophytes can still be found on normal-looking skin at 6 cm. from the margin of the lesions. It is therefore considered just as necessary to apply to preparation not only to the lesions but also on the surrounding normal-looking skin.

The results of this study justify the conclusion that topical Airol (retinoic acid) is a

preparation with a high degree of efficacy and tolerance with an acceptable irritating effect when used for tinea versicolor, especially in cases where hypopigmentation is a cosmetic problem. However, attention should be paid to the fact that patients suffering from tinea versicolor are predisposed to dermatophyte infections and that reinfection with *Malassezia furfur* may be expected at any time. Cleanliness is therefore essential for the maintenance of a healthy skin.

### SUMMARY

A clinical trial with retinoic acid (Aiol) cream 0.05% applied topically was carried out on 50 patients suffering from tinea versicolor allocated to a random procedure. The results, judged in terms of cure rate, incidence of relapse and tolerance were very satisfactory. As regards the above mentioned criteria for a successful treatment, there was no significant difference between the lotion and cream groups.

Repigmentation of the affected skin after retinoic acid occurred in a relatively shorter period compared with other anti-fungal preparations, especially when simultaneously exposed to sunlight. The therapeutic action on dermatophytes was discussed. It was pointed out that patients suffering from tinea versicolor are predisposed to dermatophyte infections and that cleanliness of the skin is a simple but essential way of preventing contamination with *Malassezia furfur*.

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