

An Effective Antidandruff Agent – IPBC

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Abstract

The purpose of this study was to determine the effect of IPBC(3-Iodo-2-propynylbutyl carbamate) on dandruff caused by the anthropophilic fungus *Malassezia furfur*.

The effects of IPBC on dandruff were examined by evaluating (a) the MIC value of IPBC using broth dilution method ; (b) the remnant antimicrobial activity of IPBC containing shampoo on skin disc ; (c) the antidandruff efficacy of 1.0 % IPBC containing shampoo in double blind clinical trial.

To investigate the remnant antimicrobial activity of IPBC against *Malassezia furfur*, guinea pig-skin disc was washed with antidandruff shampoo and then the diameter of inhibition zone per disc was measured. For clinical trial, thirty healthy volunteers, aged 25-35, participated in 4 week study. At 0, 2, 4 weeks, examinations of scaling, itching on scalp were carried out.

The MIC(Minimum Inhibition Concentration) values of IPBC range from 0.10 to 1.00 μ g/ml and it seems that IPBC is more effective in the MIC values than zinc pyrithione, selenium disulphide, piroctone olamine and comparable to ketoconazole, climbazole.

When the remnant antimicrobial activity of IPBC shampoo on skin disc was determined, 0.5% IPBC shampoo and 2.0% Ketoconazole shampoo resulted in similar antimicrobial effect. In addition, 1.0%, 2.0% IPBC shampoo was more effective than 2.0% ketoconazole shampoo.

After two and four-weeks of 1.0% IPBC shampoo treatment, there was significant reduction of scaling, itching in test group compared to control group.

On the basis of these results, it can be concluded that 1.0% IPBC is more effective than 2.0% Ketoconazole in reducing dandruff. It seems that strong capacity of drug binding to the stratum corneum plays a role in its antidandruff effect since adsorption of active ingredients on scalp is very important factor in reducing dandruff.

Key word : IPBC, Antidandruff agent,

I. Introduction

Dandruff is excessive scaling of the scalp without clinical signs of inflammation. The other common disorders which produce scaling on the scalp-psoriasis and seborrheic dermatitis-have distinctive signs of inflammation and rarely are confused with dandruff.

The etiology of dandruff and its treatment have been discussed in scores of technical communications during the past century. In an early scientific discussion of dandruff, Malassez(1) was the first to indict *Malassezia furfur* as the cause of dandruff. Over the years from 1874 to the present day, numerous authors have taken sides for or against this hypothesis. Each has presented evidence to support his contentions and his hypothesis has not been fulfilled up to present day.

IPBC(3-iodo-2-propynyl-butylcarbamate) was a highly efficient bactericide, fungicide and acaricide. For years its abilities as a harmless wood preservative have been acknowledged. According to recent FDA reports and reviews(2), IPBC is outpacing all other preservatives in the growing frequency of its use as a preservative for cosmetics and personal-care products. Also synergic effect of IPBC and other preservatives has been published(3,4).

The purpose of this study was to determine the effect of IPBC on dandruff caused by the anthropophilic fungus *Malassezia furfur*.

II. Methods and materials

II-1 Materials

3-Iodo-2-propynylbutylcarbamate (IPBC ; Arch, U.S.A) and ketoconazole (Farmax) were used for *in vitro* test and clinical evaluation. zinc pyrithione (Olin ,U.S.A and Yoshitomi, Japan), climbazole (Haarmann & Reimer, Germany), selenium disulphide (Abbott, U.S.A), piroctone olamine (Hoechst, Germany), hitokitiol (Osaca Organic Chemical, Japan), chitosan oligomer (Pacific Co., Korea), and triclosan (Ciba-Geigy, Swiss) were tested *in vitro*.

II-2 Strain and cultural media

Malassezia furfur ATCC 12087 tested *in vitro* was obtained from American Type Culture Collection and incubated in PO broth or agar media containing bacteriological peptone 0.1%, glucose 0.5%, yeast extract 0.01%, oxbile 0.4%, glycerol 0.1%, glyceryl monostearate 0.05%, whole-fat cow's milk 0.1% at 37 °C.

II-3 Preparation of guinea pig skin disks

Guinea pig skin was prepared as disks with 12-mm diameter from abdominal region of the animals, by the modified methods of Ciba-Geigy for calf skin disk preparation.

II-4 MIC test (Broth dilution method)

Compounds used in MIC test were prepared as stock solution in PO broth according to

their solubility. The stock solution was added to the first column of a 96-well microtiter plate (Falcon, U.S.A) and serially diluted (1:1) across the plate. Precultured microorganisms were inoculated to each well at a concentration of $10^5 - 10^6$ cfu/ml, and the plate was incubated at 37°C for 48 h. Tetrazolium violet (Sigma, U.S.A) was added, and the plate was checked at 4-5 h and again at 18 - 24 h. After incubation, plate was read and the last well with no growth (clear) was the MIC for that test compound.

II-5 Skin disk diffusion method

To investigate the remnant antimicrobial activity of medicated shampoos against *P. ovale* we used skin disk diffusion method, SDDM(5). Skin disk was sterilized with 70% ethanol for 30 min., hydrated, soaked in the shampoo for 3 min., and rinsed for 20 sec. with tap water. After these shampoo treatments, disks were added on the bio-assay dish (Falcon, U.S.A) poured with PO agar media inoculated with *P. ovale* at a concentration of $10^5 - 10^6$ cfu/ml. The dish was placed at 4°C for 16-18 h and incubated at 37°C for 48 h, and then diameter of the inhibition zone per disk was measured.

II-6 Clinical evaluation

30 volunteers, aged 25-35, who had been suffering from slight to severe scaling of the scalp or dandruff were enrolled in this study. For normalization, they used non-medicated (placebo) shampoo for 2 weeks prior to the study, and were randomized into three groups of 10 subjects testing one product each. After normalization, subjects of each group were instructed to use the medicated or non-medicated placebo shampoo two or three times a week for 4 weeks. 1.0% IPBC containing shampoo (group A), 2.0% ketoconazole containing shampoo (group B), and placebo shampoo (group C) were tested. Every week, subjects were evaluated the state of dandruff by three inspectors using a visual score, answered the subjective evaluation questionnaire about scaling, itching, oiliness, and irritancy, and carried out videomicroscopic visualization of their scaling. Clinical and subjective evaluation was scored according to their severity as 0, absent; 1, slight; 2, somewhat; 3, moderate; 4, severe.

III. Results

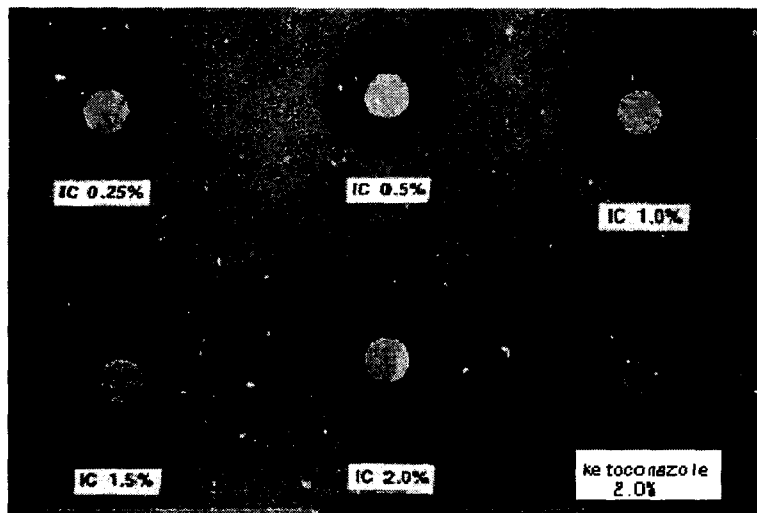
The MIC (Minimum Inhibition Concentration) values of IPBC range from 0.10 to 1.00 μ g/ml and it seems that IPBC is more effective in the MIC values than zinc pyrithione, selenium disulphide, piroctone olamine and comparable to ketoconazole, climbazole(6-8).

<Table 1> The MIC values of IPBC and other antidandruff agents on *Malassezia furfur*

Antidandruff Agent	MIC(μ g/ml)	Source
IPBC	0.10 – 1.00	Arch
Ketoconazole	< 0.10	Farmax

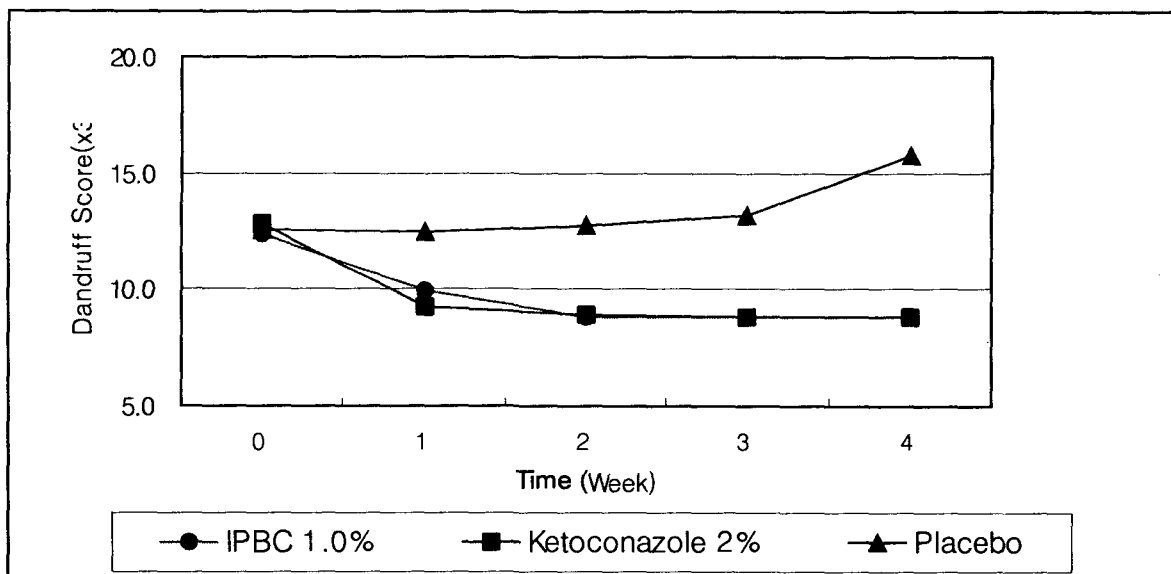
Climbazole	0.03 – 2.00	Haarmann & Reimer
Zinc Pyrithione	0.12 – 8.00	Olin, Yoshitomi
Selenium Disulphide	2.00 – 64.0	Abbot
Piroctone Olamine	16.0 – 64.0	Hoechst
Hinokitiol	20.0	Osaca Organic Chemical
Chitosan Oligomer	1000.	Pacific Chemical
Triclosan	5000.	Ciba-Geigy

When the remnant antimicrobial activity of IPBC shampoo on skin disc was determined, 0.5% IPBC shampoo and 2.0% Ketoconazole shampoo resulted in similar antimicrobial effect. In addition, 1.0%, 2.0% IPBC shampoo was more effective than 2.0% ketoconazole shampoo.

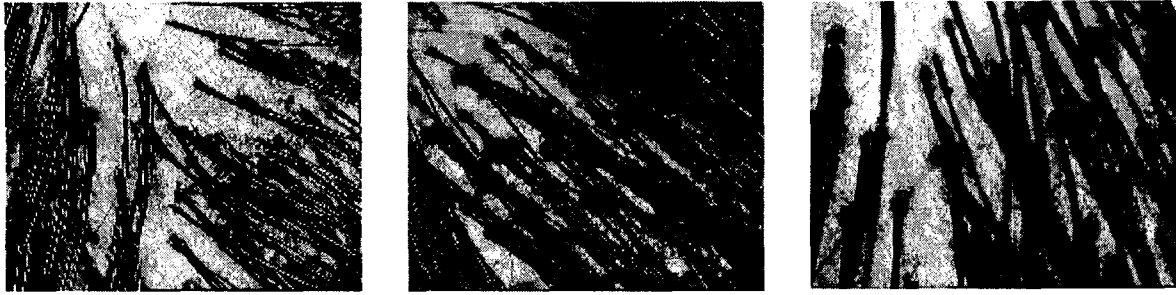


<Figure 1> The remnant antimicrobial activity of IPBC containing shampoo on skin disc.

After two and four-weeks of 1.0% IPBC shampoo treatment, there was significant reduction of scaling in test group compared to control group.



<Figure 2> Clinical evaluation of dandruff score response to treatments.



<Figure 3> Videomicroscopic visualization of the scalp about treatment of 1.0% IPBC containing shampoo.

IV. Conclusion

On the basis of these results, it can be concluded that 1.0% IPBC is more effective than 2.0% Ketoconazole in reducing dandruff. It seems that strong capacity of drug binding to the stratum corneum plays a role in its antidandruff effect since adsorption of active ingredients on scalp is very important factor in reducing dandruff.

<Reference>

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