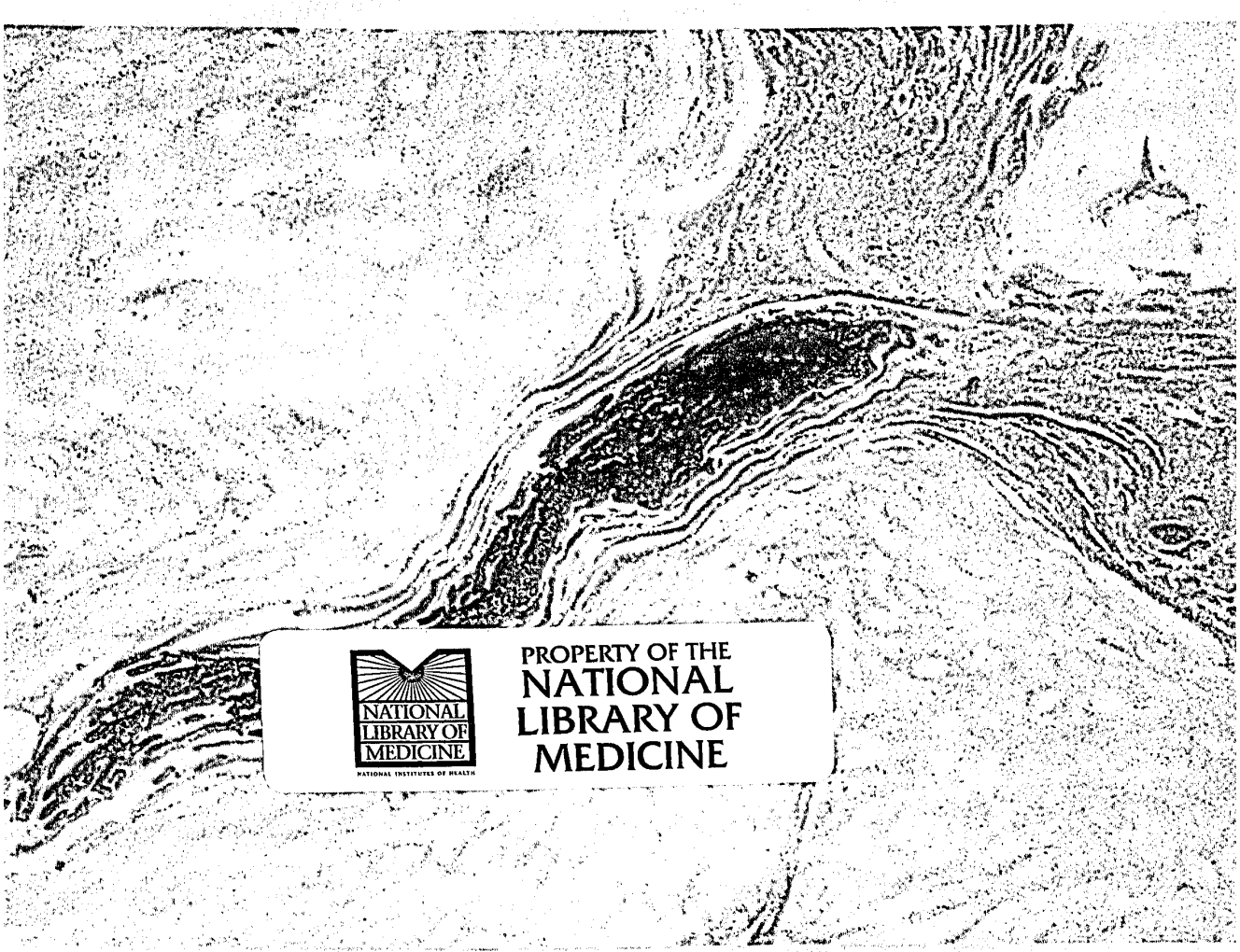
2009

Mycoses

Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Official Publication of Deutschsprachige Mykologische Gesellschaft



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Abstracted/indexed in: BIOSIS database; CAB Abstracts; Review of Medical and Veterinary Mycology; Cambridge Scientific Abstracts; Microbiology Section C; Chemical Abstracts; Current Contents/Life Sciences; Derwent Drug File; Elsevier BIOBASE/Current Awareness in Biological Sciences; EMBASE/ Excerpta Medica; Index Medicus; Index Veterinarius; MEDLINE; PASCAL; Research Alert; Science Citation Index; SciSearch; SUBIS Current Awareness in Biomedicine; Veterinary Bulletin; VINITI/ Russian Academy of Science.

Publisher
Blackwell Verlag GmbH
Wiley-Blackwell
Rotherstrasse 21
10245 Berlin, Germany
phone: +49 30 470 31-400, fax: +49 30 470 31-410
Internet Homepage: www.blackwell.de
Blackwell Verlag is now part of John Wiley & Sons.

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Submission of manuscripts
Manuscripts should be submitted online at http://mc.manuscriptcentral.com/myc. Full instructions are provided on the site.

Journal publishing manager
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Simon Tan
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e-mail: myc@oxon.blackwellpublishing.com

Offprints. For information regarding offprints please contact:
offprint@cosprinters.com
Commercial offprints: bbeyer@wiley.com

Typesetting. Scientific Publishing Services, Chennai, India

Imprint details. Printed in Singapore by Markono Print Media Pte Ltd

ISSN 0933-7407 (Print)
ISSN 1439-0507 (Online)

Information for subscribers. *mycoses* is published in six issues per year. Subscription prices for 2009 are: Premium Institutional: £447 (Europe), US$789 (The Americas), US$921 (Rest of World); Personal: €272 (Europe, Euro zone), US$352 (The Americas), £210 (Rest of World). Members of the DMykG: €204 (Europe). Prices are exclusive of tax. Australian GST, Canadian GST and European VAT will be applied at the appropriate rates. For more information on current tax rates, please go to www.wiley.com, click on Help and follow the link through to Journal subscriptions. The Premium institutional price includes online access to the current and all online back files to January 1st 1977, where available. For other pricing options, including access information and terms and conditions, please visit www.interscience.wiley.com/journals

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Periodical ID statement. MYCOSES (ISSN: 0933–7407) is published bimonthly. US mailing agent: Mercury Airfreight International Inc., 365 Blair Road, Avenel, NJ 07001, USA. Periodical postage paid at Rahway, NJ. POSTMASTER: Send all address changes to MYCOSES, Journal Customer Services, John Wiley & Sons Inc., 350 Main St., Malden, MA 02148-5020.

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VOLUME 52 JANUARY 2009 NUMBER 1

CONTENTS

CAPTION OF THE COVER ILLUSTRATION. Histopatholgical analysis of skin from untreated control (a) and guinea pigs treated with terbinafine HCl nail solutions (TNS) (terbinafine HCl 1%, dodecyl-2-N,N-dimethylaminopropionate hydrochloride 5%) (b). Sections were stained with Grocott Methenamine Silver stain. As can be seen in (a), dark-coloured Trichophyton mentagrophytes hyphae were present (arrows) in the stratum corneum of the epidermis and (b) shows the structure of intact skin from TNS-treated animals. See M. A. Ghannoum *et al.*, Determination of the efficacy of terbinafine hydrochloride nail solution in the topical treatment of dermatophytosis in a guinea pig model, pp. 35–43 in this issue.

Original article

Determination of the efficacy of terbinafine hydrochloride nail solution in the topical treatment of dermatophytosis in a guinea pig model

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Summary

Currently available topical antifungals are often not satisfactory for the treatment of nail infections, because of the inability to penetrate the nail plate. Terbinafine HCl nail solution is a novel antifungal formulation containing a nail penetration enhancer dodecyl-2-*N*,*N*-dimethylaminopropionate hydrochloride (DDAIP HCl, trade name NexACT®-88). In this study, we used a guinea pig model of *Trichophyton mentagrophytes* dermatophytosis and evaluated the clinical and mycological efficacy of different terbinafine HCl nail solutions (TNS) formulated with or without DDAIP HCl. Ciclopirox (8%) nail lacquer (Penlac®), the only Food and Drug Administration approved topical treatment for onychomycosis, was used as a comparator. Following the IACUC Guidelines, the skin of male albino guinea pigs was abraded under anaesthesia. Each animal was infected with *T. mentagrophytes* ATCC 24953 (cell suspension containing 1×10^7 conidia). The experimental animals were divided into 11 groups (five animals per group) and tested with the following formulations: vehicle control, 0.5% DDAIP HCl, 1%, 5% and 10% TNS (without DDAIP HCl), 1% TNS with 0.5%, 2.5% and 5.0% DDAIP HCl, 5% and 10% TNS with 0.5% DDAIP HCl, 8% ciclopirox nail lacquer and an untreated control group. Evaluation of clinical and mycological efficacy was performed 72 h after completion of a 7-day treatment regimen. Skin biopsy samples were processed for histopathological examination. The infected untreated control guinea pigs showed patches of hair loss and ulcerated or scaly skin and fungal invasion of hair roots. The vehicle and 0.5% DDAIP HCl treated groups showed minimal clinical efficacy (only 11% and 5%, respectively). In contrast, all three concentrations of TNS (1%, 5% and 10% terbinafine HCl) formulated with or without 0.5% DDAIP HCl showed 100% mycological efficacy by the hair root invasion test. Clinical efficacy of the 5% and 10% TNS improved with addition of 0.5% DDAIP HCl (47.4% and 73.8% vs. 68.4% and 89.5%, respectively). In addition, no fungal elements were detected in the treated guinea pig skin. All formulations of TNS resulted in a higher clinical and mycological efficacy compared with the 8% ciclopirox nail lacquer ($P = 0.0444$). In conclusion, TNS containing 1%, 5% and 10% terbinafine HCl formulated with and without DDAIP HCl demonstrated high antifungal efficacy in experimental dermatophytosis. Addition of 0.5% DDAIP HCl to 5% and 10% TNS significantly enhanced the clinical and mycological efficacy of these formulations which were superior compared with the 8% ciclopirox nail lacquer. Evaluation of the 1%, 5% and 10% TNS in clinical trials for the treatment of dermatophytosis and onychomycosis is warranted.

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Accepted for publication 25 March 2008

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