KRF043B-1
Laboratory, Main office/Team leader, theme leader

Research and Development Activity Report
May 28, 1999
Naoto Senda, Pharmacology Research Division, (seal) Senda

Theme name (code number): KP-103 (062A0)
Term: April 1999 to May 1999
Responsible parties (energy allocation): Yoshiyuki Tatsumi (30%), Mamoru Yokoo (30%)

Progress status (results, problems):
1) Establishment of guinea pig onychomycosis model and treatment efficacy of KP-103 (End)

After licensing KP-103 to Pola Chemical Industries, it is necessary to acquire a use patent for onychomycosis, in order to extend the term of the contract and authorize onychomycosis indication. Until now, the onychomycosis model was not established in any research term, so this time, establishment of the onychomycosis model for guinea pigs was tested using T. mentagrophytes SM-110 strain, for which infection in toenails is already confirmed, and the efficacy of KP-103 was investigated. The efficacy on onychomycosis was evaluated with a new method that we devised because evaluation was not possible with existing methods.

Group	Treatment frequency	Fungus-negative toenails	Average number of fungi in nails (Log CFU ± SD/foot)
Base control	15	0/10	3.00 ± 0.54
KP-103	15	0/10	2.86 ± 0.67
Lanoconazole	15	0/10	2.23 ± 0.31
Terbinafine	15	1/10	2.25 ± 0.83
Base control	20	0/10	3.23 ± 0.74
KP-103	20	3/10	1.82 ± 0.91 [a]
Lanoconazole	20	0/10	2.70 ± 0.63
Terbinafine	20	1/10	2.03 ± 0.75

[a] $P < 0.05$ vs base control

Although with the 15-time application treatment all of the drugs exhibited a decline in number of fungi in the nail, a significant fungus elimination efficacy was not confirmed. When KP-103 was applied 20 times, the number of fungi in the nail significantly declined, and complete curing was confirmed in the nails of 3 of 10 feet. On the other hand, a significant fungus elimination efficacy was not confirmed with 20 applications of lanoconazole or terbinafine. Because existing topical agents have poor penetration into the nail plate and do not exhibit efficacy, for onychomycosis, oral treatments with terbinafine and itraconazole were done. From these results, it is suggested that KP-103 is effective against onychomycosis in local administration. It is conjectured that because KP-103 as low affinity with keratin, it exhibited good penetration in the nail plate and demonstrated excellent efficacy.

This time, the world's first in vivo evaluation system for onychomycosis was established, suggesting extreme intractability in correlation with onychomycosis in humans. This method is extremely useful as a drug efficacy evaluation method for onychomycosis.

2) Conference presentations and paper preparation

Abstract submitted to the Interscience Conference on Antimicrobial Agents and Chemotherapy.

Preparing paper for submission.

Changes in plans, timing forecast, issues:

1) Confirming consistency with raw data for efficacy tests with an eye on publishing a report after the current agreement in August.

2) Based on these results, we will investigate plans for acquiring a use patent for KP-103 on nails, with the Intellectual Property Division.

Items of special note:

Affiliated chief's comments: