

Résumé

STUDIES ON ANTIFUNGAL AGENTS (I. & II. REPORT)

On several mercuric compounds, especially on Bis-ethylmercuri-phosphate.

1. Experimental Study.

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Recently, it has become clear that many organic mercuric substances have excellent antifungal activities and show therapeutic efficiencies for treatment of cutaneous fungus infections. The subject of the present paper is the fundamental study on some new mercuric compounds.

The substances examined were as follows :

- 1) Furfural-5-mercuri-chloride
- 2) Ethylmercuri-phosphate
- 3) Bis-ethylmercuri-phosphate
- 4) n-Butylmercuri-chloride
- 5) Mercuri-bis-thioglycolic acid

These were kindly supplied by Prof. T. IWAMOTO, Department of Pharmacy of our School of Medicine.

A. *In vitro* activity of the substances against 4 common species of dermatophytes.

Tubes of culture media containing serial dilutions of the compounds to be tested were inoculated with suspension of organisms and observed for growth after incubation period of 10 days at 25.0°C (fungi-static activity). Then, about 0.05 cc of culture medium from each tube was transferred to Sabouraud's agar and observed for growth over 14 days (fungicidal activity).

The results obtained were as follows :

Compound	Growth Inhibition Concentration (mcg/cc)			
	<i>T. purp.</i>	<i>T. int.</i>	<i>T. ast.</i>	<i>C. alb.</i>
1)	6.25	12.5	6.25	25.0
2)	0.195	0.195	0.39	0.39
3)	0.195	0.195	0.39	0.78
4)	0.39	0.39	6.25	6.25
5)	>100	50	>100	>100
Standard				
Sodium ethylmercuri-thiosalicylate				
	0.78	0.78	1.6	3.15

B. *In vivo* activity of the substances in the form of ointment. Suspension of organisms was rubbed in the shaved and abraded area on the flank of guinea pigs. After the ointment containing each substance in 0.2% was applied daily to the inoculated area for eight consecutive days, scales were collected and transferred to Sabouraud's agar and observed for growth after 14 days.

The results were as follows :

Compound	Ointment Base	Ratio of Growth Inhibition
2)	Hydrophilic Ointment	87.5
	Carbowax	75.5
3)	Hydrophilic Ointment	100.0
	Carbowax	100.0
4)	Hydrophilic Ointment	62.5
	Carbowax	50.0

Of 5 compounds examined, Bis-ethylmercuri-phosphate (BEMP) has demonstrated the highly potent antifungal activity *in vitro* and *in vivo* studies.

2. Clinical Study.

Because of the marked antifungal potencies of Bis-ethylmercuri-phosphate (BEMP) in the fundamental study, clinical trial was conducted using three kinds of BEMP ointment, namely, 0.2% concentrations of the drug in hydrophilic ointment (H.O.), carbowax (C.W.) and absorption ointment (A.O.). Forty six patients with cutaneous fungus infections (50 areas of involvement) were instructed to apply locally one of these ointments once daily. No other therapy, local or systemic, was given during the period of observation.

The results of treatment were as follows

- 1) 0.2% BEMP H. O. . Fifteen patients out of

17 (88.2%) were clinically cured or improved. Inflammatory side reaction was seen in 3 cases.

2) 0.2% BEMP C. W. . Of total 18 patients, 15 (83.3%) showed clinical cure or improvement. No side reaction was observed.

3) 0.2% BEMP A. O. : Eleven out of 15 patients (73.3%) were improved. Irritating reaction was remarkable in 2 patients.

Of three kinds of BEMP ointments, 0.2% BEMP carbowax ointment seemed to be highly effective and to show less side reaction. It would be a favorable drug for fungus infections of the skin.