

hydrogen acceptor in the medium, and it is hoped to bring forward evidence in support of this hypothesis.

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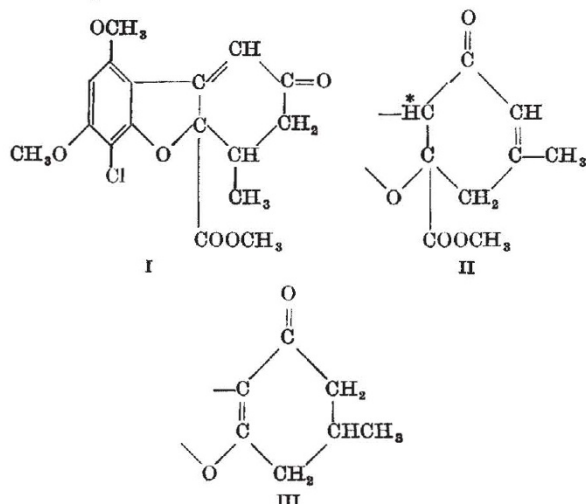
<sup>1</sup> Koser, S. A., *J. Bact.*, **8**, 493 (1923).

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### Identity of Griseofulvin and 'Curling-Factor'

WHEN *Penicillium janczewskii* is grown in liquid culture media a substance is produced which causes stunting, excessive branching and characteristic distortions in the germ tubes of *Botrytis allii* and other fungi<sup>1</sup>. The substance has been isolated and called 'curling-factor'<sup>2</sup>. When some preliminary observations<sup>3</sup> were made on the chemical and physical properties of curling-factor, the presence of chlorine was overlooked and a formula  $C_{20}H_{20}O_9$  was proposed. We find that chlorine is present and that curling-factor is identical with griseofulvin  $C_{17}H_{17}O_6Cl$ , which was isolated several years ago by Oxford, Raistrick and Simonart<sup>4</sup> from *Penicillium griseofulvum* (for curling-factor found: C 58.4; H 4.9 per cent; mol. wt. 362;  $OCH_3$  23.2; Cl 9.8 (micro) and 9.7 (macro) per cent;  $CH_3$ —(C) 4.9 per cent; calculated for  $C_{17}H_{17}O_6Cl$ : C 57.9; H 4.9 per cent; mol. wt. 352.7;  $OCH_3$  26.4 (for three  $OCH_3$ ); Cl 10.1;  $CH_3$ —(C) 4.3 (for one  $CH_3$ ) per cent). The melting point (220°) of a sample of griseofulvin which was kindly supplied to us by Prof. Raistrick was not depressed by mixing with curling-factor (m.p. also 220°); and further, griseofulvin is identical with curling-factor in its biological properties<sup>5</sup>.

Most of the chemical reactions described by Oxford, Raistrick and Simonart have been carried out with curling-factor. A mono-oxime has been prepared; hydrolytic experiments have yielded griseofulvic acid, decarboxygriseofulvic acid and norgriseofulvic acid; and oxidation gave a chloro-hydroxy-dimethoxybenzoic acid.



The formula (I) for griseofulvin was suggested<sup>4</sup> tentatively as a working hypothesis and accounts for most of the reactions very well. We find, however, that decarboxygriseofulvic acid forms complexes which appear to be oxonium salts, and the complexes are not formed until the carboxyl group is removed. The structure III would be expected to yield oxonium complexes and is readily derived from II by the migration of two hydrogen atoms after hydrolysis and decarboxylation. Other evidence seems to be in favour of the slight modification of part of structure I shown by II. Formula II, unlike I, readily explains the production of orcinol on alkali fusion. In II one of the centres of optical activity indicated by \* should undergo fairly ready racemization through enol formation. This might explain the easy production of an isomer of griseofulvin.

All the analyses were carried out by Drs. Weiler and Strauss with the exception of the chlorine estimations, for which we are indebted to Mr. J. Haslam, of I.C.I. Plastics Division.

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<sup>3</sup> McGowan, J. C., *Trans. Brit. Mycol. Soc.*, **29**, 188 (1946).

<sup>4</sup> Oxford, A. E., Raistrick, H., and Simonart, P., *Biochem. J.*, **33**, 240 (1939).

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### A Fungistatic and Bacteriostatic Red Pigment Produced by a Strain of the *Penicillium nigricans-janczewskii* Series

Two distinct strains of the *Penicillium nigricans-janczewskii* series have been isolated from Wareham Heath soil<sup>1</sup>. One of these strains, regarded as typical of the species *Penicillium janczewskii* Zal., has been shown<sup>2</sup> to produce a substance causing marked abnormality of fungus growth; this substance has since been found to be identical with the previously known mould product griseofulvin<sup>3</sup>. The other strain, distinct from *P. janczewskii* and not definitely assignable to any of the described species within the *P. nigricans-janczewskii* series, has been shown to produce fungistatic and bacteriostatic culture filtrates on Raulin-Thom medium. A red pigment possessing antibacterial and fungistatic properties has now been isolated from such filtrates.

For the production of this pigment, cultures are incubated at 25° C. on shallow layers of medium for five days, when spore germination assays show an activity of 16–32 B.A. units/ml. The culture filtrate is then extracted with chloroform and the extract evaporated to dryness. The residue is crystallized from ethanol, giving about 8 mgm. of crude red pigment per litre of culture filtrate.

By recrystallization from ethanol, glistening red needles are obtained. These begin to darken at 120° C. but do not melt at 380° C., nor is there any tendency for sublimation to occur at this temperature. The red pigment contains no nitrogen or halogen, and highly purified samples leave no ash on combustion. There are some indications of the presence of sulphur, but quantitative analysis has shown the amount present to be insignificant.