THE 'IN VITRO' EFFECT OF GRISEOFULVIN ON RINGWORM AND OTHER FUNGI.

By

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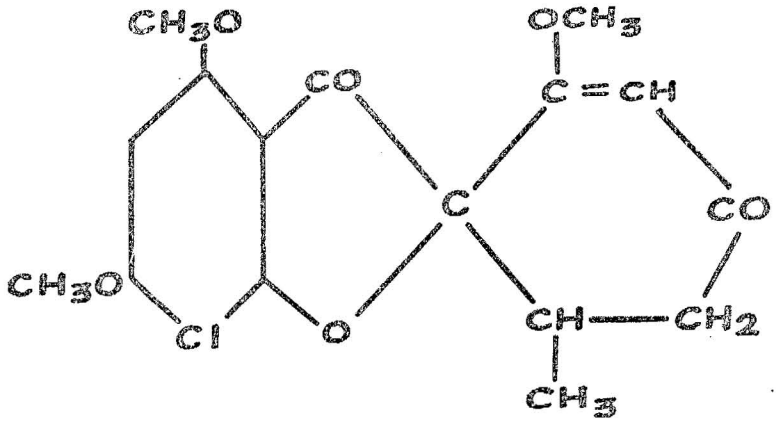
Griseofulvin, acclaimed as "a mile stone of Dermatology" by Sulzburger and Baer (1959), was first isolated by Oxford, Raistrict and Simonart (1939) from Penicillium griseofulvin Diereckx. A similar substance known as "curling factor" had been isolated from another species of penicillium by Brian and his colleagues in 1946.

Griseofulvin (C17 H1706 cl) is a white odourless, thermo stable substance having cytotoxic properties simllar to colchicine. It is relatively insoluble in water and oilve oil but is soluble in ethyi alcohol, carbo-wax 300, chloroform, acetone and butyl acetate. (Robinson et al 1960). The Chemical structure of Griseofulvin has been established by many authors. (Brian P. W. 1951, 1952, Grove et al 1951, 1952, Work T. S. 1952.).



The initial report of Williams, Martin & Sarkany (1951) and the controlled study of Blank & Roth, (1959) convincingly prove that this drug is effective in the treatment of a variety of superficial mycotic infections. In addition to these clinical studies, many 'in vitro' investigations have been conducted. Roth et al (1959), for example, investigated the inhibitory activity of this drug against a wide range of dermotophytes and other organisms.

The object of the present study was to assess the comparative inhibitory activity of griseofulvin on a wide range of common dermatophytes and saprophytes, by a special 'in vitro' technique. Various fungi which are only occasionally reported as dermatophytes e. g. M. nanum (Brock 1961), Keratinomyces ajelloi (Ehrman & Thurner 1962), T. gallinae (Gip. 1964) as well as other fungi e. g. M. distortum, M. cookei, T. ferrugineum, T. gallinae, T. Megnini T. quinckeanaum, T. terrestre and other were also included in this study.

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MATERIALS AND METHODS.

35 species of fungi were taken for this study.

The technique and method in these experiments were similar to the test tube assay procedure of Roth et al (1965) in a modified form.

Results: The minimal inhibitory concentrations of griseofulvin for the various fungi under study are shown in the following table.

TABLE

Minimal inhibitory concentrations of Griseofulvin for various fungi under study

Fungus	Minimum inhibitory concentration of Griseofulvin (ug/ml)
M. canis	3
M audouini	4
M. gypseum	8
M. nanum	4
M. cookei	6
M. distortum	6.25
T. mentagrpohytes	3
T. quinckeanaum	5
T. rubrum	4
T. Megnini	6
* T. sulphureum	3
* T. tonsurans	2
i. gallinae	3
T. verrucosum	3
T. violaceum	3.5
T. ferrugineum	3
T. concentricum	2
T. soudanense	3
T. Schoenleinii	2.5
T. terrestre	6
E. flocossum	3
K. ajelloi	6
C. albicans	No inhibition
Aspergillus fumigatus	,, ,,
A. terreus	,, ,,
A niger	,, ,,
Penicillium sp.	,, ,,
Fusarium sp.	,, ,,
Paecilomyces sp.	,, ,,
Alternaria sp.	,, ,,
Cladosprium sp.	,, ,,
Scopulariopsis sp.	,, ,,
Helminthosporium sp.	,, ,,
Mucor sp.	,, ,,
Rhizopus sp.	,, ,,

* T. sulphureum and T. tonsurans are synonyms. These were two different strains which were labelled by these names by the laboratories from where they were obtained.

DISCUSSION

Although the clinical effect of griseofulvin on dermatophytes has, by now, been established, the exact mechanism of its action "in vitro" is not fully known. It appears, however, to exert a fungostatic, rather than a fungolytic action. After oral administration, girseofulvin seems to get incorporated with the Keratin and exerts a fungostatic action (Gentles et al 1959).

In culture, the anti-fungal effect of griseofulvin was demonstrated by Brian (1947). He isolated a substance from Penicillium Janczewski, which he named as "curling factor" because its addition to the fungus caused stunting and shrivelling of its growth. Grove et al (1952) subsequently showed that griseofulvin and "curling factor" were the same.

Roth (1959) and Schwartz and Loutzenhiser (1960) demonstrated various changes, caused by griseofulvin, in susceptible cultures of fungi. In the present study the susceptible cultures showed waviness and evidence of vacuolation and autolysis in hyphae, on microscopical examination. The wide range of fungi in this study, not only included the common dermatophytes and saprophytic fungi but also those which are only occasionally reported as dermatophytes. Gip (1964) in his study, isolated from the floors of army barracks, not only T. rubrum, T. mentagrophytes, E. flocossum and M. gypseum but also M. nanum, M. cookei, T. terrestre, and K. ajelloi. The results of this study, indicate that by and large very low concentration of griseofulvin is enough for the inhibition of susceptible dermatophytes e. g. M. canis and T. tonsurans, were inhibited in a concentration of 2 ug/ml. The Saprophytic fungi were resistant to this drug. Ehrman & Thurner (1962) reported a case where onychomycosis caused by K. ajelloi was cured by the oral administration of griseofulvin although the organism showed resistance to the drug 'in vitro'. In the present study, K. ajelloi and even M. gypseum (!) have shown similar 'in vitro' resistance.

SUMMARY AND CONCLUSIONS

The effect of griseofulvin on a wide range of fungi was studied by a special "in vitro" technique. These included dermatophytes, saprophytic fungi as well as those fungi which are rarely reported as dermatophytes. The minimum inhibitory acitivity of griseofulvin on these fungi was compared.

It was seen that griseofulvin has a selective inhibitory activity on susceptible dermatophytes in very low concentrations. Non-dermatophytes were resistant to the drug.

The following organisms which have not hitherto been extensively studied, were also tested by the same technique: M. cookei, M. distortum, M. nanum, T. concentricum, T. ferrugineum, T. gallinae T. Megnini, T. terrestre, and K. ajelloi.

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