with the two plates in contact. Spacing can then be adjusted by means of the micrometers to the desired value. Collecting voltage is applied to the top plate, and for plate spacing of .5 mm or less it was found that the knee of the ionization current vs. voltage curve falls somewhat below 10 v and that the plateau extends from this point to over 350 v. In view of this, an operation point of about 40 v was chosen as appropriate for the measurements to be made.

For the dose at any one depth, readings of the ionization current are plotted vs. mm of plate spacing. This curve is essentially a straight line below .5 mm of plate spacing (Fig. 2). The slope of this line can be converted to the units of esu's of charge transferred per mm of plate spacing, and if this quantity is divided by the area of the collecting electrode as measured by the traveling microscope, a roentgen equivalent dose is obtained. The plate spacing can be adjusted by turning the micrometers to new values, and a current reading is obtained in the time needed to make a stable curve on the Brown Recorder.

The instrument shows good stability provided it is shielded by a grounded metal case, the insulated spacing between the guard ring and the collecting electrode is kept clean, and the input capacitance of the micro-microammeter is not changed. Since the micro-micro-ammeter is a current-measuring rather than a charge-measuring instrument, the actual value of input capacitance can be neglected, and a change of input capacitance will interfere only while it is taking place, the instrument again recording the true value of ionization current as soon as the input capacitance is stable.

Reference

1. FAILLA, G. *Radiology,* **29,** 202 (1937).

Crystalline Fradicin

Richard J. Hickey and Phil Harter Hidy[1]

Research and Development Department,
Commercial Solvents Corporation, Terre Haute, Indiana

Swart *et al.* (*1, 2*) have reported the presence of an antifungal agent, fradicin, in neomycin fermentation liquors. This is to describe briefly a crystalline agent, presumably fradicin, which is produced by *Streptomyces fradiae.*

The most highly purified crystalline products are light greenish-yellow. They do not show a sharp mp, but darken without definite melting between about 180° to 300° C. The solubility is less than 0.05 mg/ml in methanol, ethanol, and water, but it is greater in dioxane and in chlorinated hydrocarbon solvents such as ethylene dichloride. Fradicin also dissolves fairly readily in propylene glycol; it is practically insoluble in petroleum ether, cyclohexane, and xylene.

[1] The authors wish to acknowledge the work of O. G. Wegrich for the pathogenic fungal tests, that of J. N. Spencer for the toxicity and irritation tests, and that of J. C. Carr for microchemical analyses. The criticism of S. A. Waksman on the fungal sensitivity data is also gratefully acknowledged.

Microanalytical data indicate a tentative empirical formula of $C_{30}H_{34}N_4O_4$. *Anal.* Calcd: C, 70.01; H, 6.67; N, 10.88. Found: C, 70.29; H, 6.59; N, 10.86. This differs from actidione both chemically (*3*) and microbiologically (*2*). Neutral equivalents of 498 and 514 were obtained by two methods (*4, 5*). A molecular weight in the range of 500 was found by the Barger micro method, using dioxane. The molecular weight calculated from the empirical formula is 514.6.

Fradicin is a weak base, which forms a hydrochloride obtained as needles. The $[\alpha]_D^{25}$ of the base is about + 65° (*c* 1.0, 1,4-dioxane). Micro Zeisel analyses of the base showed 11.95% alkoxyl, probably methoxyl (Calcd: 2 CH_3O, 12.04). Alkali fusion yielded a volatile product which gave positive pine splint and Ehrlich's tests for a pyrrol. Fig. 1 shows the ultraviolet absorption spectrum of crystalline fradicin in ethanol.

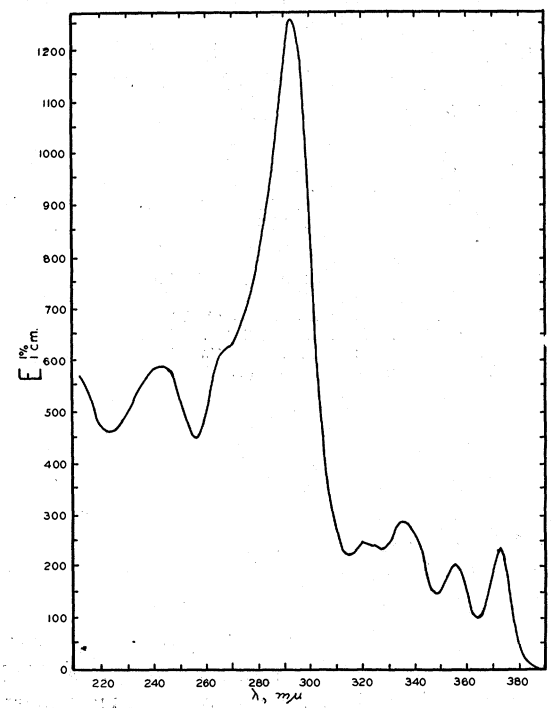

FIG. 1. Ultraviolet absorption spectrum of fradicin in ethanol.

Antifungal activity is strong at pH 7.0 and higher, but below this activity is greatly reduced. In a phenol red broth[2] at pH 7.3, activity has been demonstrated against several yeasts, including a strain of *Saccharomyces cerevisiae,* at about 0.1–0.15 μg/ml. Activity was poor against bacteria. These findings agree qualitatively with those of Swart *et al.* (*2*) for the amorphous material.

In tests using agar dilution plates[3] at pH 7.3 with 9-day incubation, inhibition was demonstrated against

[2] Difco phenol red broth base + 1% glucose + 0.1% yeast extract (Difco) + 0.1% beef extract (Difco), pH 7.3.

[3] Agar composition: peptone 1.0%, dextrose 4.0%, agar 2.0%, pH 7.3, except for *H. capsulatum,* which was studied in Campbell's medium (*6*).

some pathogenic fungi in the range of 1–10 μg/ml. Examples are given in Table 1.

TABLE 1

INHIBITION RANGE OF FRADICIN AGAINST SEVERAL PATHOGENIC FUNGI

Organism	Effective inhibition range* (μg/ml)
Candida albicans	2–4
Cryptococcus neoformans	2–4
Microsporium canis	1–3
Trichophyton mentagrophytes	3–5
Microsporium gypseum	3–10
Histoplasma capsulatum (yeast phase)	1–3

* Readings were made after 9 days' incubation.

Acute toxicity tests in mice have shown that by intraperitoneal injection, the LD_{50} was approximately 4 mg/kg. Acute oral mouse toxicity by single dose was in this same range. Some kidney ischemia was observed. Skin tests employing rabbits (*7*) have shown that, in a hydrophilic ointment, irritation was considerable at 500 μg/g, moderate at 100 μg/g, and slight at 50 μg/g.

References

1. SWART, E. A., HUTCHISON, D., and WAKSMAN, S. A. *Arch. Biochem.*, **24**, 92 (1949).
2. SWART, E. S., ROMANO, A. H., and WAKSMAN, S. A. *Proc. Soc. Exptl. Biol. Med.*, **73**, 376 (1950).
3. KORNFELD, E. C., and JONES, R. G. *Science*, **108**, 437 (1948).
4. MARKUNAS, P. C., and RIDDICK, J. A. Paper No. 22, Abs., Am. Chem. Soc. Meeting, Houston, April 1950.
5. FRITZ, J. S. *Anal. Chem.*, **22**, 578 (1950).
6. CAMPBELL, C. C. *J. Bact.*, **54**, 263 (1947).
7. DRAIZE, J. H., WOODARD, G., and CALVERY, H. O. *J. Pharmacol. Exptl. Therap.*, **82**, 377 (1944).

Electron Microscopy of Thin-sectioned Spirostomum

Harold E. Finley

Department of Zoology,
Howard University, Washington, D. C.

A great deal of attention is being devoted to the study of ultramicroscopic structures in several kinds of organisms. The author's interest in the morphology of protozoa suggested the possibility of applying electron microscopy to the heterotrichous ciliate *Spirostomum ambiguum*. Accordingly, the microsectioning method developed at the National Bureau of Standards by Newman, Borysko, and Swerdlow (*1*) was modified for *Spirostomum*. Specimens were prepared for study as follows: Live animals were concentrated in centrifuge tubes, fixed in Bouin's or Navashin's fluid, dehydrated through a dioxan series, infiltrated, embedded, sectioned according to the method cited (*1*), and studied with the 50-kv, RCA-type EMU electron microscope. Some sections were shadowed with chromium. Figs. 1 and 2 illustrate typical results obtained when specimens were prepared in the manner described.

In Fig. 1 some of the numerous particles in the

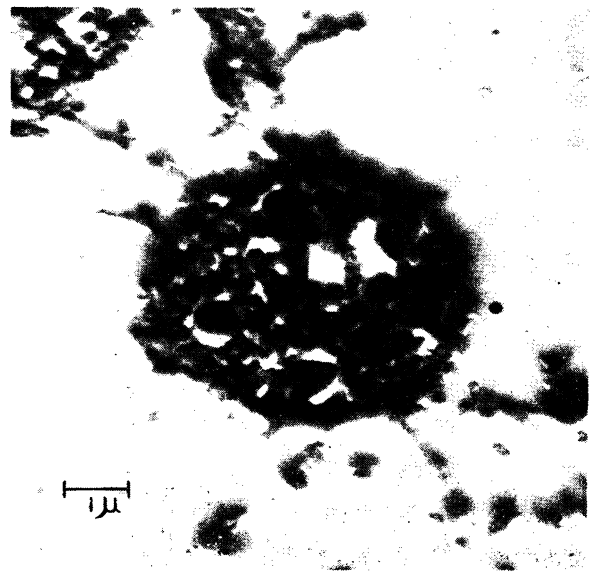

FIG. 1. Macronucleus. Chromium-shadowed (4 : 1), × 7800.

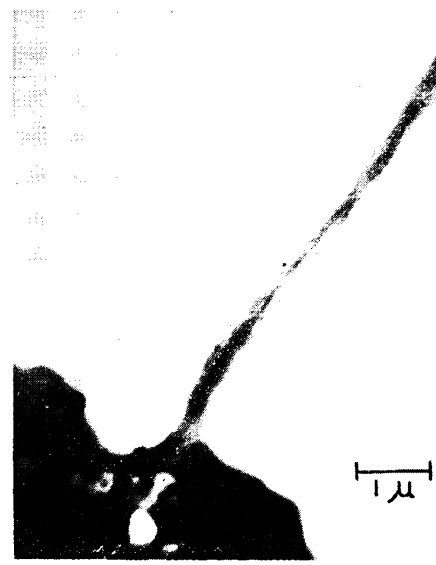

FIG. 2. Chromium-shadowed cilium, × 9000.

macronucleus are oval and others are globular in shape. Their diameters may be estimated in comparison with the shadowed particle of polystyrene latex[1] that appears in the right-central region of the figure. In making this comparison it should be remembered that the polystyrene particle was superimposed above the collodion substrate, whereas the macronuclear particles were partially imbedded in the substrate. In the macronucleus of *Spirostomum*, by suitable methods, one may discern "granular" material which gives a positive response to the Feulgen reaction; this may be a clue to the nature of the oval and globular particles shown in Fig. 1.

Fig. 2 reveals that locomotory cilia are composed

[1] Dow Chemical Co., Lot 580 G, diam approx 2600 A.