method described by Wolahan and Cutting (*1*). Results on the blood levels in subjects inhaling various doses of the micronized potassium penicillin-glucose preparation are shown in Table 1.

TABLE 1

Patient	Dosage (units of crystalline penicillin)	Interval after administration	Concentration (units/cc. citrated whole blood)
C*	30,000	½ hr.	.03
		1 "	.03
T*	30,000	½ "	.06
		1 "	.03
R*	50,000	½ "	.03
		1 "	.03
		2 "	.015
S*	50,000	½ "	.06
		1 "	.03
		2 "	.03
		3 "	.03
L	25,000	½ "	.015
		1 "	.015
		2 "	.015
M	30,000	1 " 20 min.	.06
		2 "	.06
P	30,000	1 "	.06
		2 "	.03
B	160,000	1 "	.06
		2 "	.03
		4 "	.03
		6 "	.03
		8 "	.03
		10 "	.03
		12 "	.00
O'N	90,000	½ "	.125
		1 "	.06
		2 "	.06
		3 "	.03
		4 "	.06
H	90,000	½ "	2.000
		1 "	.125
		2 "	.125
		3 "	1.000 (?)
		4 "	.060
		5 "	.060

* Normal controls. Penicillin and penicillinase controls were performed.

In all cases except one (L) where 25,000 units or more were administered, a therapeutic concentration was obtained in ½ hour and maintained for about 3 hours. After large doses (B and O'N) the therapeutic levels are maintained for approximately 10 hours. In two cases studied it was found that 10–15 per cent of the dose administered was excreted in the urine in the first hour.

Any soluble therapeutic agent which can be produced in the solid state or which can be chemically precipitated or physically combined with glucose, β-lactose, lactose, etc. may be micronized and used in the manner described. Some of the agents meeting these requirements are: the sulfonamides; antibiotic agents such as penicillin and streptomycin; hormones such as insulin and estrone; antihistamine drugs such as Benadryl; vasoconstrictors such as neosynephrine and ephedrine; narcotics such as codeine and dilaudid; biologicals such as immune human globulin, vaccines, etc.; various medicinal compounds such as cough mixtures; and numerous others. These materials may be used individually or in compatible combinations, with or without a vehicle.

In certain diseases principally those in which a high local concentration of the agent at site of the infection or reacting organ is of great importance, this method of therapeutics is particularly advantageous. These include certain diseases of the respiratory tract, topical application where indicated, allergic states, and urinary tract infections. The method is also useful in the prophylaxis of venereal diseases, acute rheumatic fever, common carrier states, and the prevention of postoperative pulmonary infections.

This method of administering penicillin glucose mixtures has been used in more than 40 cases of various diseases where penicillin therapy was indicated. The clinical and bacteriological response to treatment has been excellent. Patients prefer this type of treatment to injections or aerosol. By the incorporation of from 2 to 5 mg. of Benadryl/dose of penicillin glucose mixture (200 mg.) there have been no local sensitivity reactions to penicillin in the last 35 cases.

This preliminary report is presented for the purpose of stimulating further study of the method described. Several studies of the suggested applications of the method are in progress at the University of Rochester School of Medicine and Dentistry by members of various departments of the University.

References

1. Wolahan, M. B., and Cutting, W. C. *J. lab. clin. Med.*, 1945, **30**, 161.

A Simple Device to Increase Background Contrast in Photomicrography

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In the photography of small insects it has been considered necessary in this laboratory to find a means of intensifying the blackness of the background. A simple microscope attachment was therefore constructed to make possible the desired contrast between the photographed object and the background. This device, which is essentially the physicists' "black body," consists of a cavity with a small opening and with interior walls of low reflectance. The opening is placed beneath the specimen to be photographed and provides a background of very nearly zero reflectance, since the light that enters the opening is absorbed within the cavity.

To construct this cavity, it was found convenient to use the black bakelite cover of a microtessar lens container, but any cylinder of comparable dimensions and lined with a nonreflective black substance should be satisfactory. A disk of black photographic paper with a ¼-inch hole cut in its center was glued over the open end to provide the small opening referred to above. This simple device will ride on the condenser lens and can be elevated into position immediately below the

[1] The writer wishes to thank R. E. Worley, of the Physics Department at this University, for his review and criticism of this paper.

microscope slide holding the specimen. A felt pad attached to the bottom of the device will eliminate the possibility of scratching the condenser lens.

With the ¼-inch hole in position beneath the specimen, a deep black background is provided even when the specimen is strongly illuminated with flood lamps. Thus, in the case of predominantly "black" insects, sufficient contrast is provided between the reflective "black" of the insect and the nonreflective black of the background formed by the cavity.

As it was constructed, the device (Fig. 1) is 1¼ inch in diameter and has a depth of ¾ inch. However, the use of any

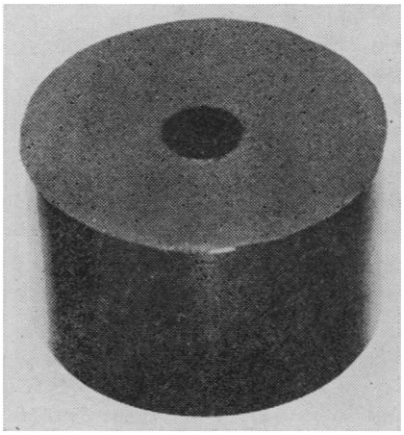

FIG. 1

properly blackened box with flat, removable lids having various hole sizes will serve a similar purpose when objects of greater dimensions are to be photographed.

Crystalline Dihydrate of Calcium Ascorbate

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Szent-Györgyi (*3*), in investigating vitamin C, mentioned that the solubility of the calcium salt excluded its identity with that of the acid studied by Bertrand and others.

Hirst, *et al.* (*1*) prepared the calcium salt by adding a slight excess of calcium carbonate to the aqueous solution of ascorbic acid. The solution was evaporated to dryness in a desiccator. The dry residue was then triturated with alcohol when a neutral salt was obtained which had a pale yellow color and gave an aqueous solution with a rotation of $[\alpha]_D^{19} + 91$. Analysis showed a calcium content of 9.9 per cent, as compared with the theoretical 10.2 per cent, for $(C_6H_7O_6)_2$. No analysis of the carbon or hydrogen was stated, and apparently the substance was not crystalline.

Calcium ascorbate, prepared as a cream-colored dry powder, has been made in considerable quantites for medicinal preparations. However, because of its hygroscopic property, this soon took up moisture when exposed to a humid atmosphere and became gummy, decomposing to an orange-colored product. It was thus unsuitable for practical use.

One of the writers (S. L. R.) developed the stabilized solutions of calcium ascorbate which have since been widely used. Study was continued, however, to secure a stable, dry form of calcium ascorbate that could be employed for oral therapy. This has apparently been attained in the dihydrate of calcium ascorbate.

While investigating the production of a more stable form of calcium ascorbate we have succeeded in crystallizing this important salt from water. The crystals obtained are white, are much more stable than the uncrystallized salt, and have remained dry and white when exposed for several months to the humid atmosphere of the laboratory.

Due to the known tendency of ascorbic acid solutions to oxidize and undergo further decomposition, solutions of the calcium ascorbate were were not allowed to stand for long periods in water or alcohol, nor was the temperature of the solutions allowed to rise much above 30°. It was found necessary to dry the crystals with absolute alcohol and to remove the alcohol quickly to avoid oxidation of the crystals, with subsequent coloration.

METHOD

The first product to approach the crystalline salt in composition was obtained by precipitation in acetone. Sixty grams of ascorbic acid was dissolved in 140 cc. of hot water, the solution cooled to 30°, and 16.3 grams (a little less than ½ mole) of calcium carbonate added slowly with stirring. The solution was filtered with suction to remove a small residue and the excess of carbon dioxide. The aqueous solution was run in a thin stream by means of a pipette into 3,000 cc. of acetone with constant stirring. Some gum, in addition to a flocculent precipitate which at first was in suspension, formed on the bottom of the beaker. The gum was kneaded with the stirring rod and, on standing overnight, became brittle. This was broken up, the acetone decanted, and the precipitate washed with 300 cc. of fresh acetone. The material was filtered, ground in a mortar, rubbed up in about 200 cc. of ether to remove the excess of acetone, and filtered with suction to remove ether. When dry, it contained 9.3 per cent calcium.

One gram of the calcium ascorbate obtained by precipitation from acetone was rubbed up in 0.5 cc. of water. Crystals formed which, under the microscope, appeared as prisms.

Crystalline calcium ascorbate was next prepared from water, using as seed the first crystals obtained. One hundred and twenty grams of ascorbic acid was dissolved in 280 cc. of hot water, the solution cooled to about 25°, and 32.6 grams (a little less than ½ mole) of calcium carbonate added with stirring. The solution was filtered with suction, as before, to remove the small residue and excess carbon dioxide, and the filtrate was evaporated *in vacuo* to a thin syrup of about 170-cc. volume. On seeding and stirring, a crystalline mass was obtained which, after standing no longer than an hour, was filtered with suction, the crystals then being rubbed up with 200 cc. of absolute alcohol, refiltered, and washed with an additional 50 cc. of alcohol to remove excess moisture. Alcohol was removed by drawing air through the filter and then spreading the crystals on filter paper to dry. The yield was 71.9 grams, or 49.5 per cent of the theoretical. Higher yields were obtained when the solution was evaporated to a thicker syrup.

The crystals remained white and dry for months on exposure to the humid atmosphere of the laboratory.