Paralysis is regularly prevented by brewers' yeast, is cured by a water extract of yeast,[3] and has responded promptly (8–12 hours) to synthetic biotin[4] therapy in seven attacks in four dogs. The biotin was dissolved in physiological saline and administered subcutaneously. The therapeutic dose is approximately 100 gamma per kilo.

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PRELIMINARY NOTE ON THE INACTIVATION OF ANTIBIOTICS

DURING the course of investigations on antibiotic substances of plant origin[1] an antibiotic active against both Gram positive and negative organisms was isolated from *Allium sativum*. During the course of chemical studies of this antibiotic, the reaction with cysteine was investigated. It was found, as is the case with penicillin, that the antibiotic is rapidly inactivated by cysteine.

A number of other antibiotics of thallophyte and spermatophyte origin available in this laboratory were tested in the presence of cysteine. In every case, cysteine gave complete inactivation or marked diminution of antibiotic activity. Gram-positive antibiotc activity is more susceptible to cysteine inactivation than the Gram-negative activity.

The following antibiotics were inactivated: penicillin, citrinin, gliotoxin, clavacin (patulin or claviformin), pyocyanine; the active principles of *Allium sativum, Ranunculus acris* and *R. bulbosus, Erythronium americanum, Asarum reflexum,* Bassica species and *Arctium minus*. The antibiotic principles of *Allium sativum, Erythronium americanum, Asarum reflexum* and *Arctium minus* will be described in greater detail later.

The testing procedure was as follows: Water solutions of each of the antibiotics were divided into two portions. One portion was used as a control and to the other was added solid sodium biocarbonate adequate to maintain a pH of approximately 7 and cysteine hydrochloride. The solutions were allowed to stand for 30 to 60 minutes, then tested for antibiotic activity against *Staphylococcus aureus* and *Bacillus paratyphosus* A by the Oxford cup method.

This antagonistic effect of cysteine was similarly displayed by cysteine esters (methyl and ethyl), but not by S-methyl cysteine, methionine, alanine or serine. Other –SH compounds such as glutathione and thioglycollic acid had either no effect or a much weaker action.

This inactivation is especially unusual in the light of the widely different chemical types of antibiotics involved. The nature of the reaction of cysteine with some of the antibiotics is known; others are being investigated. In the known instances, cysteine reacts irreversibly with the antibiotics. However, this may not be true of all the antibiotics. Quantitative relationships of the antagonistic activity of cysteine and related compounds are being studied and will be reported later. It is suggested that possibly the fundamental mode of action of certain classes of antibiotics involves their ability to interfere with the normal function of sulfhydryl groups in bacterial metabolism. This has already been observed in some specific instances as by Fildes,[2] in his investigation of the mode of action of mercury as an antibacterial agent; by Eagle,[3] who observed that the anti-spirochetal action of arsphenamine could be counteracted by cysteine; and by Atkinson[4] in her work with penicidin.

That the sulfhydryl group is essential to cell proliferation has been demonstrated and discussed by Hammett.[5,6]

This note is published with the desire that other investigators having access to different antibiotics will test such substances for inactivation by cysteine.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

ENHANCED PRODUCTION OF PENICILLIN IN FLUID MEDIUM CONTAINING CELLOPHANE[1,2]

THE observation was made that young colonies of *Penicillium notatum* in fluid medium show a tendency to develop nearer the side walls of the vessel than

[3] Kindly supplied by Dr. C. N. Frey, of the Fleischmann Laboratories, Standard Brands, Inc., New York, N. Y.

[4] Kindly supplied by Dr. D. F. Robertson, of the Merck Company, Inc., Rahway, N. J.

[1] This work was begun before the appearance of the article by Osborn, *Brit. Jour. Exper. Path.*, 24: 227, 1943, and as a result, many of the plants tested have been duplicated.

[1] From the Laboratories of Bacteriology, The Mount Sinai Hospital, New York, N. Y.

[2] The author wishes to acknowledge thankfully the accurate and capable assistance of Miss Alice Fisher.

[2] Fildes, *Brit. Jour. Exper. Path.*, 21: 67, 1940.

[3] Eagle, *Jour. Pharmacol.*, 66: 436, 1939.

[4] Atkinson, Stanley, *Australian Jour. Exper. Biol. Med. Sci.*, (4)21: 249, 255, 1943.

[5] Hammett, Hammett, *Protoplasma*, 15: 59, 1932.

[6] Hammett, Chapman, *Growth*, 2: 223, 297, 1938.