the tubercle bacillus. Against *Staphylococcus* and *Streptococcus* it has only slight activity, and against *Escherichia coli* none at all.

The active agent, whatever its nature, is very stable, for it is not completely destroyed even when autoclaved at a pressure of fifteen pounds for fifteen minutes. The filtrates from cultures kept at 28° C. for three months still show activity, and samples of the residue from ether extraction kept at 8° C. for the same length of time lose none of their potency.

Preliminary tests on mice have indicated that the crude extract is relatively non-toxic. Between 6 and 8 mgms can be tolerated by a mouse.

The experiments thus far have shown that there is an additional fungus of the Aspergillus group from the culture filtrate of which a substance can be obtained that definitely inhibits the growth of *M. tuberculosis in vitro*. It seems desirable, before attempting to establish the value of the antibiotic substance in experimental tuberculosis to obtain it in a more pure form. Studies are in progress to this end.

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## THE EFFECT OF CYSTEINE ON STREPTOMYCIN AND STREPTOTHRICIN

THE recent communication of Cavallito and Bailey[1] describing the complete or partial inactivation of a large number of antibiotics by cysteine prompted us to test the action of the latter on streptothricin and streptomycin concentrates.[2] It was found that streptomycin is inactivated by cysteine, whereas streptothricin is not. Streptomycin is also inactivated by 2-aminoethanethiol but not to any significant extent by thioglycollic acid. The inactivation experiments were carried out by adding neutral solutions of the organic sulfur compounds to known amounts of streptomycin or streptothricin dissolved in neutral phosphate buffer. After storing for several hours, the solutions were tested for antibiotic activity against *Bacillus subtilis* by the Oxford cup method.[3]

TABLE 1

EFFECT OF ORGANIC SULFUR COMPOUNDS ON ACTIVITY OF STREPTOMYCIN AND STREPTOTHRICIN SOLUTIONS

| Concentration of organic sulfur compound (mg/ml) | Streptomycin assay (units/ml) | Streptothricin assay (units/ml) |
|---|---|---|
| Control (phosphate buffer) | 49 | 52 |
| *Cysteine HCl* | | |
| 0.13 | 39 | .. |
| 0.25 | 29 | .. |
| 0.50 | 4 | 42 |
| 1.00 | 0 | .. |
| 2.50 | .. | 52 |
| 5.00 | .. | 54 |
| *2-Aminoethanethiol HCl* | | |
| 0.50 | 12 | 40 |
| 2.50 | 4 | 57 |
| 5.00 | 0 | 59 |
| *Thioglycollic Acid* | | |
| 0.50 | 31 | 41 |
| 2.50 | 39 | 40 |
| 3.00 | 26 | 30 |

[1] Cavallito and Bailey, SCIENCE, 100: 390, 1944.

[2] The activity of streptomycin concentrates varied from 80 units/mg to 600 units/mg; the activity of the streptothricin was 440 units/mg.

The difference in behavior of streptomycin and streptothricin toward cysteine is of interest and of particular significance in view of the microbiological similarity of the two substances.[4] With the use of cysteine one can not only differentiate the two antibiotics but estimate the relative amounts of each in mixtures of the two (Table 2).

TABLE 2

EFFECT OF CYSTEINE ON MIXTURES OF STREPTOMYCIN AND STREPTOTHRICIN

| | Streptomycin added (units/ml) | Streptothricin added (units/ml) | Cysteine hydrochloride added (mg/ml) | Assayed activity (units/ml) |
|---|---|---|---|---|
| Solution I ... | 25 | 25 | 0 | 45 |
| Solution II .. | 100 | 0 | 2 | 0 |
| Solution III . | 100 | 8 | 2 | 9 |
| Solution IV . | 100 | 15 | 2 | 17 |
| Solution V .. | 50 | 50 | 1.3 | 45 |

The cysteine inactivation of streptomycin can be reversed by iodine; presumably cystine is formed during this process. To our knowledge, this is the first recorded instance of reversible cysteine inactivation of an antibiotic. The regeneration of the antibiotic activity of streptomycin solutions containing cysteine was carried out by shaking such solutions with small amounts of a carbon tetrachloride solution of iodine until no further decolorization occurred. The solutions were aerated to remove the organic solvent before assay. The recovery of activity was quantitative.

The observations thus far made indicate that the inactivation of streptomycin is reversible, not a property of the sulfhydryl group alone, nor is it limited to cysteine. A mechanism postulating either a reversible chemical reaction between the two substances or a competitive effect on metabolic processes would be consistent with these observations.

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[3] Foster and Woodruff, *J. Bact.*, 45: 408–9 (1943).

[4] Waksman, Bugie and Schatz, *Proc. Staff Meetings Mayo Clinic*, 19: 537–548, 1944.

## THE MECHANISM OF PAIN IN TRIGEMINAL NEURALGIA[1]

TRIGEMINAL neuralgia (tic douloureux), an episodic, recurrent, unilateral pain syndrome, occurs for the