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Silver-Coated Nylon Fiber as an Antibacterial Agent

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A blend of nylon fiber and silver-coated nylon fiber (the latter known as X-static) was used in these experiments. This fiber was bactericidal when bacteria were exposed to it directly or to an extract derived from its prior incubation in salt solution. At ambient temperatures, a rapid exponential decrease of survival occurred, usually after a delay of approximately 1 h. The rate of killing (decrease of survival) increased with an increase in X-static percentage of the fiber blend, temperature of fiber extraction, concentration of Tris buffer present during extraction, and temperature at which bacteria were exposed to the extract. When bacteria were exposed to the extract at 37°C as opposed to ambient temperature, there was no delay in onset of killing. *Escherichia coli* was generally the indicator organism tested, but comparable results were also found for *Pseudomonas*, *Klebsiella*, *Staphylococcus*, and *Streptococcus* species. The rate of killing increased with increasing silver ion concentration of the fiber extract, as determined through atomic absorption spectrophotometry. The rate of killing was greater and the onset was earlier with an extract containing silver ions from fiber than with a salt solution containing the same concentration of silver ions from silver nitrate. Studies of the kinetics of ion release suggested that X-static may be an effective, sustained-release antibacterial agent.

Silver ion (Ag^+) is a significant resource for topical therapy by virtue of its antiseptic properties (6) and concomitant low toxicity to mammalian cells (1). Of special importance has been its role in the prevention and treatment of burn infection, an area of clinical practice particularly dependent upon local as opposed to systemic drug administration (4, 7).

Characteristics sought for any agent under consideration for topical burn therapy are that it be continuously released to the wound site without the necessity for frequent and painful readministration, and that—after losses, if any, through inactivation by components of the wound tissue and exudate—the drug remain present at a concentration sufficient for its antimicrobial effect (4). The first method of Ag^+ delivery attempted in this context (0.5% $AgNO_3$ solution) does not completely satisfy these requirements inasmuch as ionization occurs very rapidly and a large proportion of the Ag^+ becomes unavailable for inactivation of bacteria due to its high affinity for biologically active anions in the wound environment. Principal among these is chloride ion (derived from sodium chloride) with which it rapidly combines to form insoluble silver chloride. Prolonged $AgNO_3$ administration in this manner thus presents the danger of hypochloremia and hyponatremia through a net flux of sodium chloride to the site (6). Resultant losses of free Ag^+ necessitate frequent reapplications of $AgNO_3$, a procedure that demands considerable nursing care time (4, 7). $AgNO_3$ administration carries with it further disadvantages in that the involved tissues turn black due to deposition of reduced silver, and absorbed nitrate can lead to methemoglobinemia (6).

The introduction in 1968 of silver sulfadiazine (SSD) as an antimicrobial agent in burn therapy (3) circumvented these problems. Administered usually as a 1% cream, SSD has low solubility in body fluids, dissociating into Ag^+ and sulfadiazine slowly and continuously over time (7) at concentrations selectively toxic to microorganisms (6). SSD therefore requires less frequent application than does $AgNO_3$. Administered in this manner, the Ag^+ does not react with local anions and thus does not undergo significant inactivation (4, 5). The sulfadiazine moiety is itself bacteriostatic (6, 7). Conveniently, SSD remains white upon contact with body tissue (4, 6).

Although SSD is the most widely used drug in burn management today, it does have some disadvantages. It is commonly applied once or twice each day in a procedure which is still time-consuming and sometimes distressing to the patient (12); adverse reactions occasionally occur (6); some concern for the body burden of the absorbed drug has been noted (12); and, with the emergence of SSD resistance, the compound is not effective in all cases (4, 7). Thus, research has been continued in an effort to find improved methods of SSD delivery (9, 11, 12) or alternatives to SSD altogether (2, 4, 7). One such study involved in vitro experiments testing the antimicrobial activity of a commercially produced silver-coated nylon fabric (2). In the present study, we performed in vitro experiments on the bactericidal effect of a similar silver-coated nylon fiber, X-static (Sauquoit Industries, Inc., Scranton, Pa.).

MATERIALS AND METHODS

Fibers. A blend of uncoated nylon and silver-coated nylon fibers was used in these studies. The fibers are woven and sold for use in settings requiring reduction of static charge. The uncoated component is a 7.6-denier nylon fiber (0.0033 cm in diameter). To produce the silver-coated component (X-static), silver (12% by weight) is added during manufacture by means of an electrodeless plating process. The X-static and uncoated nylon fibers may be blended in any proportion to vary the amount of silver present; the X-static/uncoated fiber ratios for these experiments were 5.5/94.5, 8.6/91.4, 20/80, and 25/75. Frequently, 0.25 g of fiber composed of 8.6% X-static (i.e., 22 mg of X-static containing 2.64 mg of Ag^+) was used.

Bacteria. *Escherichia coli* WU36-10, a derivative of strain B/r that is auxotrophic for leucine and tyrosine (10), was

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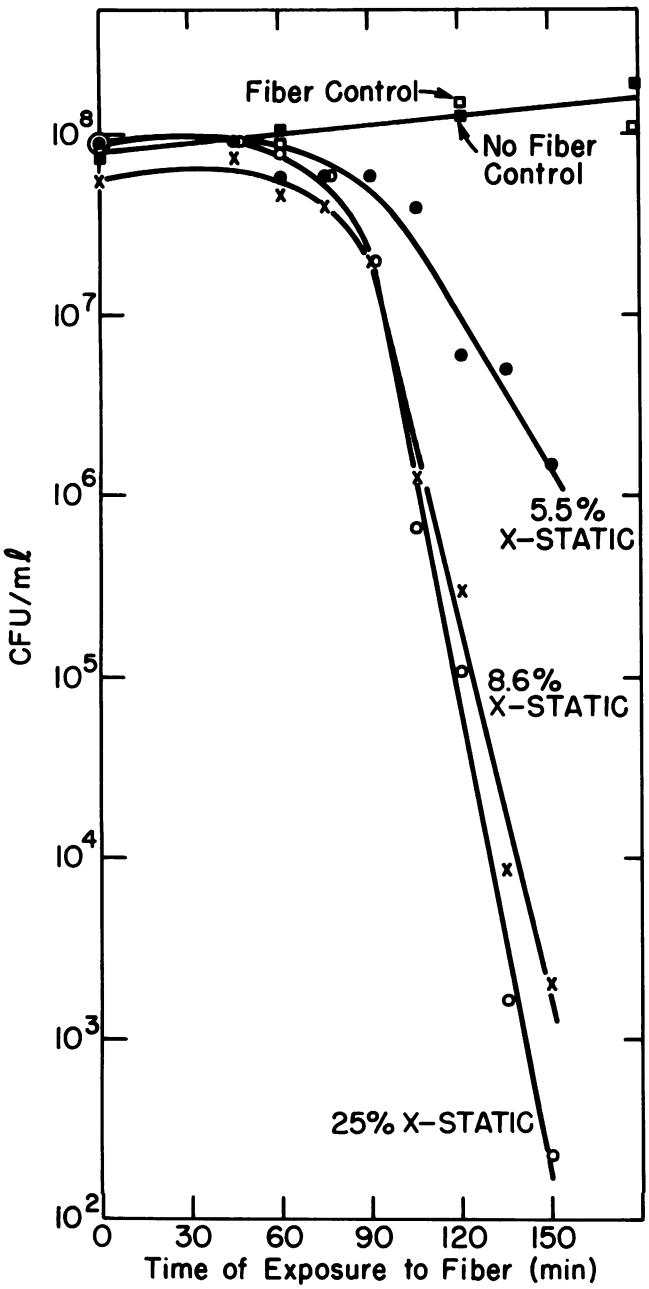

FIG. 1. Effect of varying the silver content of fibers. *E. coli* cells were grown to an optical density of 0.2, after which five 5-ml portions were centrifuged and each was suspended in 5 ml of salt solution. To four of these were added 0.25 g of fiber containing 0 (fiber control), 5.5, 8.6, or 25% X-static. Tube 5 received no fiber (no fiber control). Cultures were maintained at 26°C, and samples were removed at the times indicated for determination of CFU. The CFU of surviving bacteria per milliliter are plotted on a logarithmic scale as a function of their time of exposure to the fiber.

used in most experiments. Other bacteria tested were *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 13883), *Staphylococcus aureus* (PSU 240A), *Staphylococcus epidermidis* (ATCC 14990), *Streptococcus lactis* (PSU 253), and *Streptococcus agalactiae* (ATCC 12386), supplied by Mary Jane Tershak from our departmental culture collection. In preparation for the experiments, most bacteria were grown with aeration at 37°C in Luria broth (10 g of tryptone, 5 g of yeast extract, 0.5 g of NaCl, 1 liter of water) to a concentration of 10^8 cells per ml (optical density of 0.2 at 620 nm) (Spectronic 20; Bausch & Lomb, Inc., Rochester, N.Y.). *Streptococcus* species were maintained in an atmosphere of 5% CO_2–95% air.

Susceptibility assay. Except as otherwise indicated, bacteria were exposed to Ag^+ present in an extract prepared in advance by incubation of fibers in a salt solution (8.5 g of NaCl, 0.5 g of KCl, 1 liter of water) for 1 h with aeration to facilitate mixing. The incubation temperature was varied according to experimental conditions, and upon termination of the incubation period, the fibers were removed. After growth to an optical density of 0.2, bacteria were centrifuged and suspended in an equal volume of the fiber extract (5 ml for each experimental condition). Immediately upon cell suspension and at intervals up to 3 h thereafter, 100-μl samples were removed, diluted in a nutrient medium (10 g of tryptone, 5 g of yeast extract, 7 g of NaCl, 1.5 g of KCl, 0.5 g of $MgSO_4 \cdot 7H_2O$, 1 liter of water), and plated on the same medium solidified with 1.5% agar. Unless otherwise noted, cells were maintained at room temperature (26°C) during the sampling period. Plates were incubated overnight at 37°C, and visible colonies were counted the next day to determine the number of CFU present at each sampling time.

Silver ion quantification. The Ag^+ concentration of the fiber extracts was determined through use of an atomic absorption spectrophotometer (model 303; The Perkin-Elmer Corp., Norwalk, Conn.). A silver cathode lamp was used at a wavelength of 338.5 nm. Fresh solutions of $AgNO_3$ (ACS reagent; Apache Chemicals Inc.) containing 1.0, 2.0, 3.0, and 4.0 μg of Ag^+ per ml were used for preparation of a standard curve of percent absorption versus Ag^+ concentration. Percent absorption readings for fiber extract solutions were then evaluated against the standard curve for determination of their Ag^+ concentration. To reduce variability, three readings were taken and averaged for each measurement; when possible, three fiber incubation tubes were prepared per experimental condition, and the resulting solutions were combined before bacterial suspension.

RESULTS

Effect of varying the silver content of fiber. Preliminary experiments indicated that the silver-coated fiber was bactericidal to *E. coli* incubated in its presence in growth medium. The following experiment elaborated on these results by varying the X-static content of the fiber from 0 to 25% and substituting a salt solution for the growth medium previously employed. Bacteria and fibers were present together throughout the sampling period. Samples were removed and assayed for CFU (Fig. 1). After a delay of approximately 1 h after exposure to X-static-containing fiber, the number of surviving bacteria rapidly decreased. The rate of killing increased with an increasing percentage of X-static. No bactericidal effect was observed in the absence of fibers or in the presence of fibers that were not silver coated. The increase of CFU for control cultures was due to residual cell division after removal of bacteria from the growth medium.

Fiber incubation temperature. It was postulated that if the antibacterial effect was due to the action of Ag^+ displaced from the fiber, then it would also be observed in an extract prepared by preincubation of the fiber in a salt solution from which the fiber (8.6% X-static) was removed just before resuspension of cells (Fig. 2). The experiment also compared the bactericidal effects of fiber extracts prepared at temper-

atures ranging from 26 to 42°C. It was found that the extracts were indeed bactericidal to *E. coli* and that higher temperatures of fiber incubation resulted in proportionately earlier killing onset and a faster rate of killing. However, the onset of killing was later and the rate of killing was lower when bacteria were maintained in extract than when bacteria were brought into direct contact with the fiber (Fig. 1 and 2).

Temperature during bacterial exposure to fiber extract. We tested bacterial susceptibility to the fiber extract under two different temperature conditions. After incubation of fibers at 37°C, the resulting extract was used to suspend *E. coli* cells which were subsequently maintained at either 27 or 37°C (Fig. 3). An increase in the postextraction temperature to 37°C increased the rate of killing by a factor of approximately 2, and there was no delay in killing onset. The time required for the CFU to decrease by 10-fold was 22 min for *E. coli* exposed to the fiber extract at 37°C and 43 min for exposure at 27°C.

Fiber incubation in horse serum. Fibers were incubated in horse serum rather than salt solution to determine whether a similar bactericidal effect would be found with a solution that is more comparable to wound exudate. Fibers were incubated for 1 h at 37°C; bacteria were suspended in the extract as before, and the suspension was maintained at 26°C (Fig. 4). The rate of killing observed was similar to that found when fibers were incubated at 27°C in salt solution (Fig. 3). The time required for the CFU to decrease by 10-fold was 45 min for the serum extract relative to 43 min for fiber extraction with salt solution.

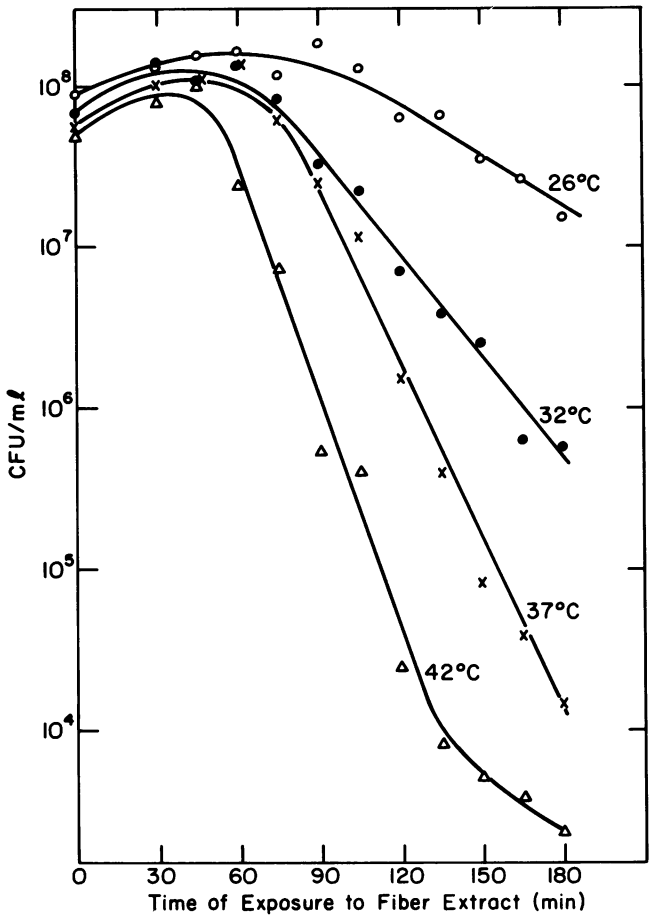

FIG. 2. Effect of fiber incubation temperature on bactericidal action. Four tubes containing 10-ml volumes of salt solution and 0.25 g of fiber composed of 8.6% X-static (22 mg of X-static) were incubated with aeration for 1 h at 26, 32, 37, and 42°C, respectively. The fibers were then removed, and the resulting extracts were used to suspend *E. coli* which had been grown to an optical density of 0.2 and centrifuged. Samples were removed at the times indicated for determination of CFU per milliliter.

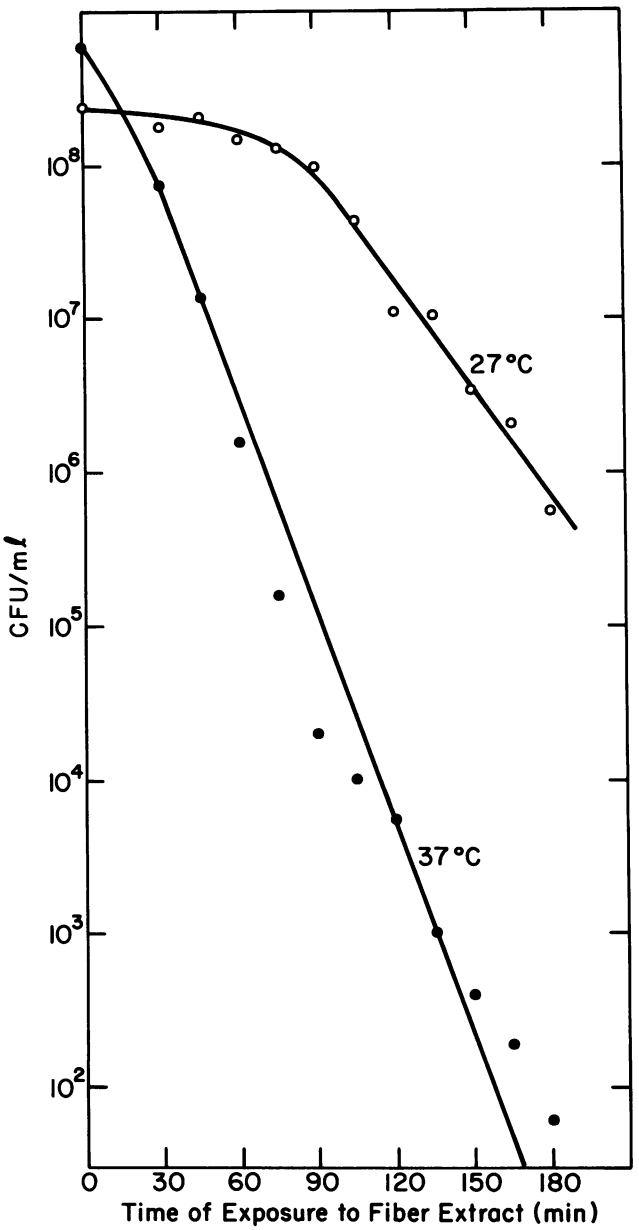

FIG. 3. Effect of temperature at which bacteria are exposed to fiber extract. Three tubes containing 0.11 g of fiber, which had a 20% X-static content (22 mg of X-static), in 10-ml volumes of salt solution were aerated for 1 h at 37°C. The fibers were then removed, and the three resulting extracts were combined and used to suspend two centrifuged 5-ml portions of *E. coli* which had been grown to an optical density of 0.2. One tube of suspended bacteria was subsequently maintained at 27°C, and the other was maintained at 37°C. Samples were removed at the times indicated for determination of CFU per milliliter.

Effect of fiber extract on selected human pathogens. A bactericidal effect was also observed for the pathogens (Fig.

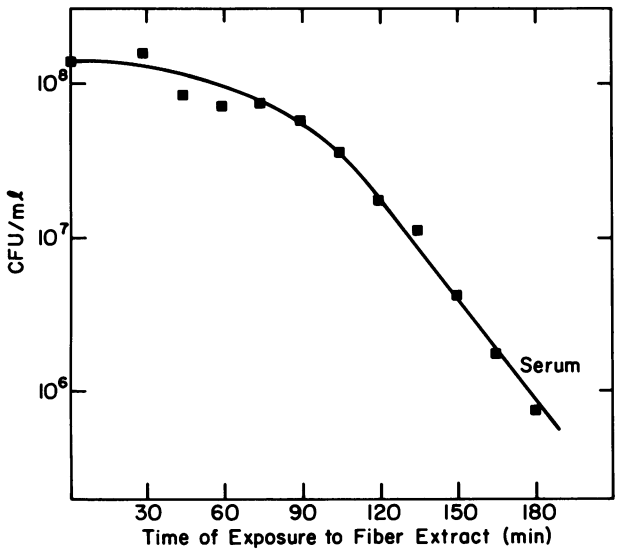

FIG. 4. Fiber extraction in the presence of horse serum. A 10-ml tube of horse serum (Flow Laboratories, Inc., McLean, Va.) containing 0.25 g of fiber composed of 8.6% X-static (22 mg of X-static) was incubated with aeration for 1 h at 37°C. The fibers were then removed, and 5 ml of the resulting extract was used to suspend a centrifuged 5-ml portion of *E. coli* which had been grown to an optical density of 0.2. Bacteria were subsequently maintained at 26°C, and samples were removed at the indicated times for determination of CFU per milliliter.

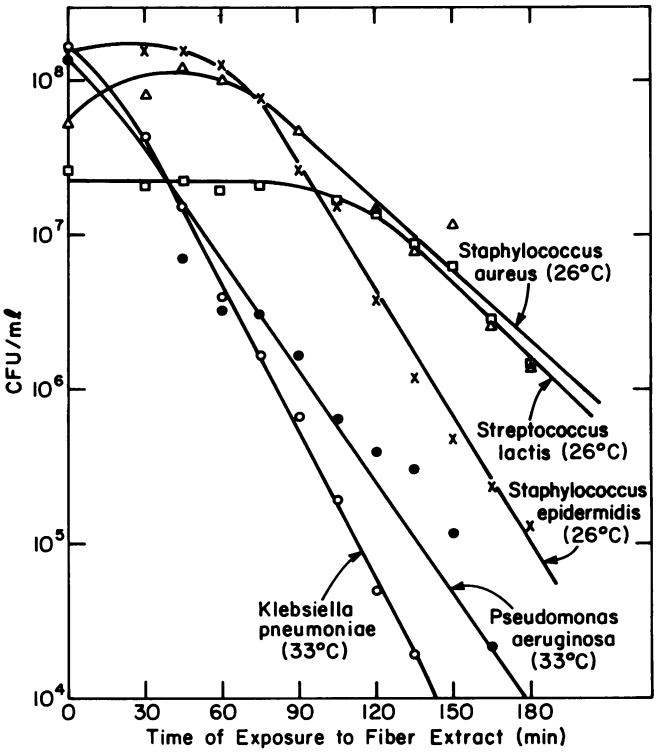

FIG. 5. Effect of fiber extract on selected human pathogens. Tubes containing 10-ml volumes of salt solution and 0.11 g of fiber composed of 20% X-static (22 mg of X-static) were aerated at 37°C for 1 h. The fibers were then removed, and 5 ml of the resulting extract was used to suspend a centrifuged 5-ml portion of each pathogen culture (grown to 0.2 optical density). Bacteria were subsequently maintained at the temperatures indicated, and samples were removed at 15-min intervals for determination of CFU per milliliter.

5). Times required for the CFU to decrease by 10-fold were in the range of 28 to 68 min. For *P. aeruginosa* and *K. pneumoniae* incubated in the fiber extract at 33°C, the killing onset was immediate, as was the case for *E. coli* incubated at 37°C. When other test strains were incubated in extract at 26°C, there was a delay in killing onset. The lag time for *S. lactis* was longest (90 min), presumably because streptococcal species readily form chains; that is, the survival of any member of a chain leads to formation of a colony. A similarly long lag time (105 min) was observed for *S. agalactiae* (data not shown).

Tris buffer concentration. When phosphate buffer at pH 7.4 was incorporated to ensure that uniform pH was maintained, there was no change in the kinetics of survival curves (data not shown). However, increasing concentrations of Tris buffer over a range of 0 to 50 mM increased the rate of killing and decreased the time before killing onset (Table 1). Without fiber, 50 mM Tris had no effect on bacterial survival. The concentration of Ag^+ released from X-static to the salt solution, as determined by atomic absorption spectrophotometry, was found to increase with higher concentrations of Tris (Table 1); thus, Tris facilitates Ag^+ release.

Comparison of bactericidal effects of Ag^+ from fiber and from silver nitrate. The bactericidal effect of an Ag^+-containing fiber extract was compared with that of an equivalent concentration of Ag^+ (1.58 μg/ml) from $AgNO_3$ (Fig. 6). With the fiber extract, there was an earlier onset and greater rate of killing than with the Ag^+ from $AgNO_3$. In an additional experiment, the bactericidal action of fiber extract was compared with that of the same extract to which sodium nitrate had been added just before suspension of cells (the nitrate concentration was equivalent to that introduced by $AgNO_3$ previously). The resulting survival curves were similar (data not shown); consequently, the nitrate ion was eliminated as a possible inhibitory factor for the antimicrobial action of $AgNO_3$.

Kinetics of Ag^+ release. The kinetics of Ag^+ release from the fiber to the salt solution over a 24-h period were investigated (Fig. 7). At 24 h, 2.15 μg of Ag^+ per ml was present in the extract. Approximately 75% of this amount had been released during the first 1 h, with a gradual inhibition of release thereafter. In a 1-h extension of the experiment to probe the possible source of this inhibition, it

TABLE 1. Killing rate as a function of Tris buffer and silver ion concentration[a]

Tris concn (mM)	Ag^+ concn (μg/ml)	Time (min) required to decrease survival by 10-fold
0	1.24	147
1	1.34	122
10	1.53	26
50	1.93	13

[a] Four tubes, each containing 0.25 g of fiber (8.6% X-static content [22 mg of X-static]), were aerated at 26°C for 1 h in 10-ml volumes of salt solution with various concentrations of Tris buffer as indicated. The fibers were then removed, and 5 ml of each resulting extract was used to suspend a centrifuged 5-ml portion of *E. coli* previously grown to an optical density of 0.2. Samples were removed at various times for determination of CFU per milliliter. The Ag^+ concentration was determined by atomic absorption spectrophotometry.

was found that the fiber previously incubated for 24 h yielded to fresh salt solution a quantity of Ag^+ comparable to that released initially (Fig. 7), while new fiber incubated in the 24-h extract released considerably less.

Kinetics of Ag^+ uptake by *E. coli*. The kinetics of Ag^+ removal by *E. coli* from a fiber extract (containing 1.62 μg of Ag^+ per ml) over a 1-h period were examined. Removal was rapid at the outset but slowed to reach a plateau at approximately 45 min (Fig. 8). The extract Ag^+ concentration was reduced by 0.98 μg/ml after 60 min, representing a loss of 5.47×10^{15} silver ions to the cells. The initial number of bacteria (determined by plating and CFU counting) was 6.5×10^8, and thus Ag^+ uptake was 8.4×10^6 ions per cell. In a replicate experiment, the binding per bacterium was 1.6×10^7, giving an average for two experiments of 1.2×10^7 ions per cell. After being exposed to Ag^+ for 1 h in this manner, cells were centrifuged and suspended in fresh salt solution (containing no Ag^+) to investigate the pattern of ion release. Negligible Ag^+ was detected in the solution at 30 and 60 min, thus suggesting that Ag^+ uptake is irreversible over this time frame in this system.

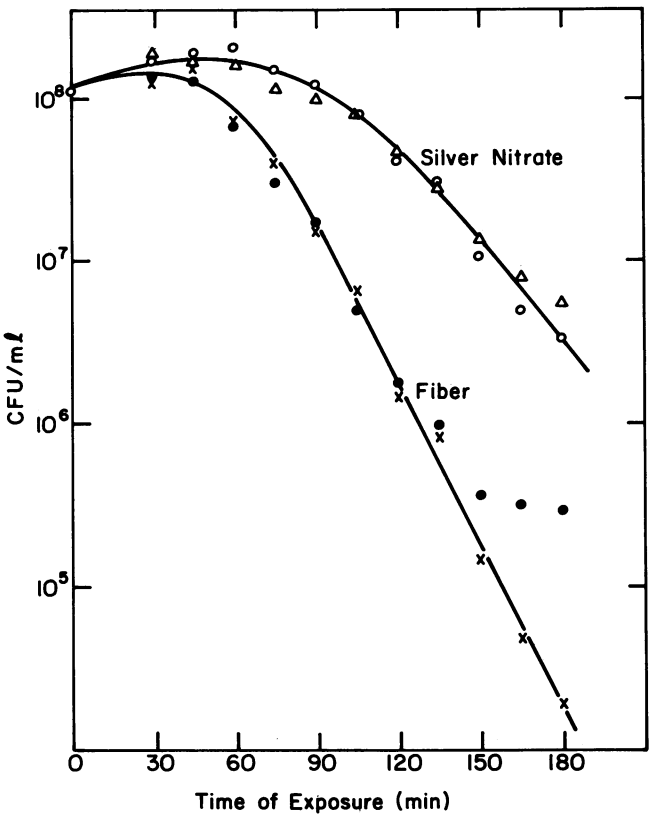

FIG. 6. Comparison of the bactericidal effect of Ag^+ from fibers and from $AgNO_3$. Atomic absorption spectrophotometry determined that the concentration of Ag^+ in an extract resulting from a 1-h incubation of fiber containing 22 mg X-static in 10 ml of salt solution at 37°C with aeration was 1.58 μg/ml. Another salt solution containing 1.58 μg of Ag^+ per ml from $AgNO_3$ was then prepared. Two 5-ml portions of centrifuged *E. coli* previously grown to an optical density of 0.2 were suspended in fiber extract, and two were suspended in the salt solution containing Ag^+ from $AgNO_3$. Both sets of duplicate tubes were maintained at 26°C, and samples were removed for determination of CFU per milliliter at the times indicated.

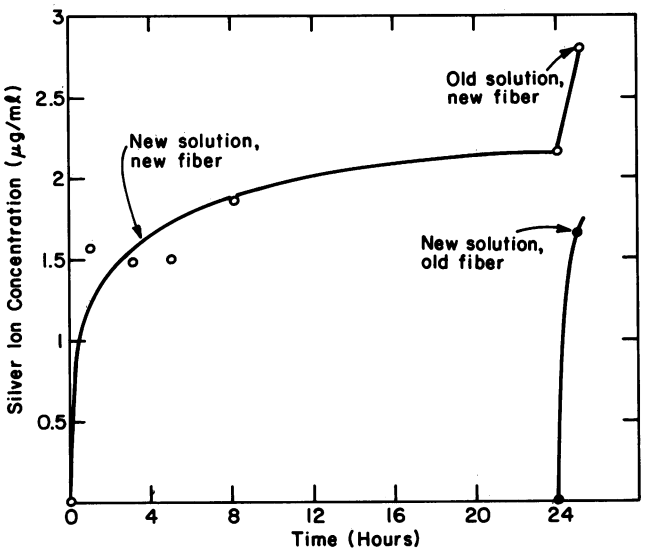

FIG. 7. Kinetics of Ag^+ release. Tubes containing 10 ml of salt solution and 0.11 g of fiber composed of 20% X-static (22 mg of X-static) were aerated at 37°C. After 1, 3, 5, 8, and 24 h, extracts were drawn off, and their Ag^+ concentrations were measured by atomic absorption spectrophotometry. Extracts from three tubes were pooled for each data point to minimize error. At 24 h, two 10-ml portions of the pooled extract were added to two additional tubes, each containing 0.11 g of fresh fiber composed of 20% X-static; these were aerated at 37°C for 1 h, and the Ag^+ concentration was again measured (old solution, new fiber). At the same time, 10 ml of fresh salt solution was added to the old fiber, which had previously undergone a 24-h extraction, and incubation with aeration proceeded at 37°C for an additional 1 h; Ag^+ concentration was then measured (new solution, old fiber).

DISCUSSION

The silver-coated nylon fiber (X-static) was bactericidal when test organisms were either exposed to it directly in nutrient broth or resuspended in an extract formed by its previous incubation in salt solution. This effect was also observed in experiments with horse serum. Onset of bacterial inactivation was temperature dependent, occurring almost immediately at 37°C, but having a delay of 1 h or more within the 26 to 27°C range, an effect which possibly reflects enhanced membrane fluidity and faster Ag^+ uptake at the physiological temperature. Although *E. coli* was the organism most frequently tested, similar experiments performed with *P. aeruginosa*, *K. pneumoniae*, *S. aureus*, *S. epidermidis*, *S. lactis*, and *S. agalactiae* yielded comparable results, suggesting that X-static possesses broad-spectrum antibacterial properties.

It is probable that Ag^+ released from the fiber is partly, if not wholly, responsible for the bactericidal effect. There is qualitative support for this assumption in that an enhanced rate of killing was found with experimental conditions expected, a priori, to release more Ag^+ to solution (increasing concentration of X-static and higher temperatures of fiber incubation in salt solution). It was also found in experiments not reported here that reduction of salt concentration below the physiological level during fiber extraction results in reduced bacterial mortality, presumably because fewer sodium ions are available to replace Ag^+ on the fiber carrier molecule. Additional quantitative support for the bactericidal effect of Ag^+ is that increased Tris molarity resulted in measurably higher concentrations of Ag^+ in the fiber extract

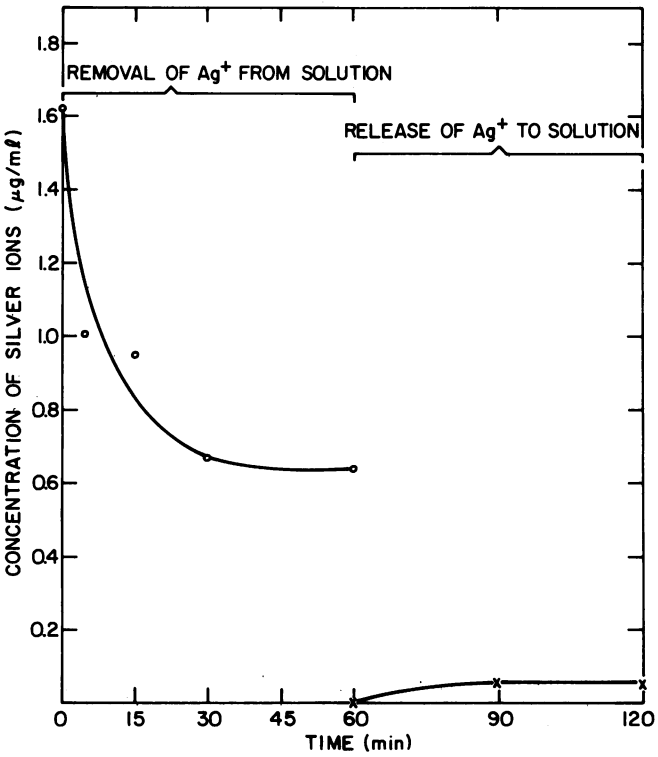

FIG. 8. Kinetics of Ag^+ uptake by *E. coli*. Three tubes, each containing 10 ml of salt solution and 0.11 g of fiber, composed of 20% X-static, were aerated at 37°C for 1 h. The resulting extracts were then combined, and the Ag^+ concentration, as determined by atomic absorption spectrophotometry, was found to be 1.62 μg/ml. Five 5-ml portions of centrifuged *E. coli* (grown to an optical density of 0.2) were each suspended in 5 ml of this fiber extract. At 5 min after suspension, one cell culture was recentrifuged, and the Ag^+ concentration of its supernatant was measured. The remaining tubes were treated in a similar manner at 15, 30, and 60 min after suspension. Cell pellets from the two tubes centrifuged at 60 min were suspended in 10 ml of fresh salt solution and portioned into two new tubes. At 30 and 60 min, these were centrifuged, and their supernatants were assayed for Ag^+. Cells were maintained at 37°C without aeration during the experiment.

and higher rates of bacterial killing. Tris acts during the fiber incubation period presumably by facilitating Ag^+ release. Further quantitative evidence for the antibacterial effect of Ag^+ can be found in a comparison of data in Table 1 (10 mM Tris) and the fiber extraction curve of Fig. 6. In the former case, 22 mg of X-static incubated in salt solution with 10 mM Tris for 1 h at 26°C gave rise to a Ag^+ concentration of 1.53 μg/ml and a 10-fold decrease in CFU over a 26-min period. In the latter case, 22 mg of X-static, incubated in plain salt solution for 1 h at a higher temperature (37°C), gave rise to a comparable Ag^+ concentration (1.58 μg/ml) and a similar 10-fold increase in CFU (30-min period). Thus, a given Ag^+ concentration yielded a reproducible decrease in survival, regardless of the protocol for Ag^+ extraction. The presence of an enhancer species in the fiber extracts cannot yet be ruled out, however; in an experiment comparing the bactericidal effect of the fiber extract with that of a salt solution containing the same amount of Ag^+ derived from $AgNO_3$, there was an earlier onset and greater rate of killing with the extract. Although it is possible that an inhibitor of the bactericidal effect was present in the $AgNO_3$ preparation, it is more likely that some additional molecule(s) released from fiber to the incubation medium may possess antimicrobial properties. Since the uncoated nylon component of the fiber is not bactericidal, additional antimicrobial elements may have been introduced during the silver-coating process. Should any such molecules be present, their human pharmacological properties should be investigated.

During a 24-h incubation of fibers in salt solution at 37°C, approximately 75% of the total Ag^+ extracted was released during the first 1 h. When fibers previously incubated for 24 h were incubated for an additional 1 h in fresh salt solution, the Ag^+ release response was equivalent to that observed during the first 1 h of the 24-h incubation. On the other hand, when a 24-h extract already containing Ag^+ at 2.15 μg/ml was incubated with fresh fibers for an additonal 1 h, the increment in Ag^+ was only a fraction of that released during the first 1 h. Release was thus limited more by the accumulation of Ag^+ in the extract than by the amount available in the fiber. Only 0.6% of the total silver content of the fiber was extracted after 1 h of incubation in fresh salt solution. These findings suggest that X-static may function in vivo as a reservoir for release of Ag^+ on demand. Bacterial removal of Ag^+ from an extract containing 1.6 μg/ml was approximately 10^7 ions per cell during 1 h of incubation at 37°C, with uptake kinetics consistent with those reported by Modak and Fox (8). Thus, bacteria, X-static, and wound exudate would represent a dynamic system within which the equilibrium may be moved in favor of Ag^+ dissociation from the fiber as long as bacteria continue to remove Ag^+ from solution. Other elements potentially affecting the equilibrium, however, include competitive binding of Ag^+ to tissue and exudate anions (e.g., chloride, sulfhydryl, carboxyl, phosphate, and amino groups) (6) and the degree to which the wound is in communication with other body fluids. The effectiveness of X-static in this milieu awaits assessment in an animal burn model.

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