

Studies on the development of a vaginal preparation providing both prophylaxis against venereal disease and other genital infections and contraception

*II- Effect in vitro of vaginal contraceptive and non-contraceptive preparations on *Treponema pallidum* and *Neisseria gonorrhoeae**

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Since 1956, when the incidence of infectious syphilis and gonorrhoea began to rise following its marked decrease after World War II, the upward trend has continued with little variation to the present time. In the U.S.A., of the reportable infectious diseases, syphilis and gonorrhoea combined are second only to influenza and far exceed streptococcal sore throat, tuberculosis, poliomyelitis, and other diseases which are now commonly regarded as a threat to mankind (Webster, 1970). Gonorrhoea is now in the epidemic state not only in the United States, but in many countries throughout the world. It has long been recognized that the actual number of cases of venereal disease (V.D.) is much greater than that reported by physicians; in the United States only 10 per cent. of cases of V.D. are reported, according to a nationwide study done by the American Social Health Association (1969), and in some urban areas one out of every ten of the sexually active population acquires gonorrhoea annually (Kraus and Webster, 1971). Other diseases known to be transmitted during sexual intercourse, such as scabies and pediculosis pubis, are said to be increasing in frequency. It has been contended that the removal of fear of pregnancy by the increasing availability and use of oral contraceptive pills and intrauterine devices has contributed to the increase of promiscuous sexual activity, and has thus possibly become a new factor facilitating the spread of V.D. (Idsoe and Guthe, 1967). Another factor is that changes in ethical, moral, and behavioural codes are taking place—the so-called 'sexual revolution'. Venereal disease and unwanted pregnancy alone or together may result from unprotected sexual intercourse, and it is hypothesized that the use

of an intravaginal contraceptive preparation combined with an intravaginal agent for prevention of infection would simultaneously reduce the frequency of both conditions. Considering the importance of this matter, we have undertaken a research project as described previously (Cutler, Utidjian, Singh, and Arnold, 1971).

The study described here is our first report on laboratory work directed to a search for a combined agent with contraceptive and prophylactic properties.

Material and methods

Most of the preparations tested in this study were purchased directly from the market. Some of the products were received from the manufacturers in response to requests by letter. The various tests used for this study were adopted from the United States Food and Drug Administration Methods for Testing Antiseptics and Disinfectants (1931). Dilutions of various preparations were made in physiological saline solution and unless otherwise specified, a mechanical mixer (Vortex) was used for proper mixing and for preparing the serial dilutions.

Harvest of spirochaetes

A rabbit infected with pathogenic *Treponema pallidum* (Nichols strain) received from the Venereal Disease Research Laboratory, Center for Disease Control, Atlanta, Georgia, provided the source of the strain which has been maintained by regular passage in rabbits for subsequent testing. At the peak of acute orchitis, the rabbit is killed by injecting air into the ear vein. The testicles are removed aseptically, sliced, and minced into small pieces. Physiological saline solution with 20 per cent. rabbit serum is added in a quantity of 15–20 ml. for each pair of testicles. The spirochaetes are extracted by shaking the flask for 1½ hours, using a low-speed mechanical shaker at room temperature. Then the material is centrifuged for 15 minutes at 110× G and the supernatant suspension of treponemes is removed. The harvest

is considered satisfactory for the test if ten or more actively motile spirochaetes are present per 40× darkfield in each of five different fields. For regular passage and maintenance of *T. pallidum*, 0.2 to 0.5 ml. of the spirochaete harvest is injected by the intratesticular route into a healthy normal rabbit. The next spirochaete harvest from the injected rabbit is made in about 11 days at the time of acute orchitis.

TECHNIQUE FOR TESTING SPIROCHAETICIDAL EFFECT

The spirochaeticidal property of various test samples was studied according to the previously reported methods of Arnold and Cutler (1956) as well as those of Turner, Hollander, and Schaeffer (1953). Each test sample was diluted to 50, 20, 10 and 1 per cent. concentrations (weight/volume) with physiological saline. For preliminary screening, one drop of *T. pallidum* suspension was placed on the microscope slide next to one drop of the diluted test sample. The two drops were mixed with an applicator stick and the stop-clock was started for timing. The coverslip was then placed and the slide was examined by darkfield microscopy. The time required to immobilize spirochaetes was noted and recorded. 1 to 1.5 minutes were required for the preparation and thorough darkfield examination of the five different fields of each wet smear slide; accordingly the dilutions of the test sample that were effective in rendering the spirochaetes non-motile within 1 to 1.5 minutes were further tested. For this purpose a more quantitative method was used in which 0.5 ml. *T. pallidum* suspension was mixed with an equal volume of diluted test sample. At various intervals slides were prepared and examined for the motility of spirochaetes. The time required for the immobilization with each dilution was recorded. Physiological saline solution was used as a control and the number of spirochaetes and their motility was recorded at the end of the experiment. The pH of the saline control solution was adjusted with 1N HCl or NaOH to that of the test sample.

Neisseria gonorrhoeae CULTURE

For preliminary studies the isolates of *N. gonorrhoeae* from the local Health Department V.D. Clinic were used. However, for the purpose of this study, a stock culture was prepared by lyophilizing a bacterial suspension which was obtained from 24-hour-old bacterial colonies by washing with Trypticase Soy Broth (BBL) containing 10 per cent. rabbit serum. Micro-organisms were grown on chocolate agar or Thayer-Martin (TM) selective medium in a CO₂ incubator at 37°C. The plates of Thayer-Martin medium were prepared and used as described by Thayer (1970). The inoculum was prepared by washing a 24-hour culture from one plate with 1 ml. Trypticase Soy Broth and adding additional broth to bring it to a standard density 60 ± 5 per cent. transmission as determined by Colorimeter, B and L spectronic '20' at 620 mμ. The total number of micro-organisms was also determined by the standard plate dilution method on TM medium. *N. gonorrhoeae* cultures were identified by the oxidase test and Gram-staining and were confirmed by sugar fermentation test.

TECHNIQUE FOR TESTING BACTERICIDAL EFFECT

Two methods were used for determining the bactericidal and bacteriostatic effect of test samples on *N. gonorrhoeae* cultures. Undiluted, and 50, 20, 10, and 1 per cent. (W/V) concentrations of contraceptives and vaginal antiseptics were prepared and tested as follows. In preliminary studies the chocolate agar and the TM selective medium were compared. The same results were obtained by using these two media, but because several products were found contaminated as originally received in jars from different companies, it was decided to use TM selective medium.

(a) Time exposure method

To 1 ml. of various dilutions of test samples of the preparation under study, 0.1 ml. of bacterial culture suspension containing 10⁵ to 10⁶ organisms was added and mixed. After intervals of 1, 5, and 10 minutes, the mixture was inoculated by streaking on TM selective medium plates, using a 3-mm. wire loop. The plates were incubated in a CO₂ incubator at 37°C. and read after 24 hours. The concentration of test material which completely inhibited the visible growth of *N. gonorrhoeae* after the period of exposure was taken as the effective concentration for this exposure interval.

(b) Plate dilution method

1 ml. of each dilution of the test sample was added to 9 ml. of melted TM medium at about 50°C., mixed, and poured into 60 × 15 mm. Petri dishes. After the plates were dry, they were inoculated by streaking with a 3-mm. wire loop from a bacterial suspension containing 10⁵ to 10⁶ Colony Forming Units (CFU) per 0.1 ml. The plates were incubated in a CO₂ incubator at 37°C. and read after 24 hours. The lowest concentration of test material completely inhibiting the visible bacterial growth was considered the end-point.

Results

EFFECT ON MOTILITY OF *T. pallidum*

Twenty contraceptive and seventeen non-contraceptive vaginal antiseptic preparations were tested for their spirochaeticidal effects on *T. pallidum* *in vitro*. The results in Table I show the effective concentration of contraceptives which inhibited the motility of actively motile *T. pallidum*. As shown in Table I the various contraceptives are grouped according to the concentrations required to immobilize spirochaetes within 1 to 1.5 minutes. Only two contraceptives were effective at 1 per cent. concentration and were placed in Group A. The pH of these two contraceptives at 1 per cent. concentration were 6.2 and 7.1 respectively. Group B included twelve different contraceptives all of which were effective at 10 per cent. concentration. The pH alone within this range was not responsible for reducing the motility of spirochaetes as judged by the controls in this range. Three contraceptives (Group C) were effective at

TABLE I Dilutions of contraceptives required to immobilize *T. pallidum* suspension within 1 to 1.5 minutes*

Group	Name of contraceptive	Concentration (per cent.)	No. of contraceptives	pH range
A	Emko Concentrate + B, Ortho Cream	1	2	6.2-7.1
B	Certane Vaginal Jelly, Contra Foam, Cooper Creme, Delfen Cream, Delfen Foam, Emko Concentrate, Emko Concentrate + A, Finesse, Immolin Vaginal Cream-Jel, Lorophyn Suppositories, Ortho Gynol Jelly, Preceptin Gel	10	12	4.6-7.5
C	Contra Creme, Lanesta Gel, Ramses Vaginal Jelly	20	3	5.5-6.9
D	Koromex A Vaginal Jelly, Milex, Crescent Jelly	50	2	5.5-5.6

*Control from pH 4.6 to 7.5 did not immobilize spirochaetes in 5 minutes

20 per cent. concentration and two at 50 per cent. (Group D).

The results with non-contraceptive preparations tested for this purpose are shown in Table II. Several of these test samples were to be found to be spirochaeticidal by the criterion of motility.

Nine preparations (non-contraceptive Group B) out of seventeen immobilized spirochaetes within 1 to 1.5 minutes. The pH of test samples in Group B ranged from 3.5 to 7.2. The more alkaline preparations, with the exception of one (Group E), were effective at high dilution (1 per cent.) as shown in Group A; the pH of two preparations was 8.8 and 9.4.

EFFECT ON GROWTH OF *N. gonorrhoeae*

All these contraceptives and other preparations were tested for their inhibitory effect on the growth of *N. gonorrhoeae*. Two types of tests were used for this study and results are shown in Table III and IV for contraceptives and non-contraceptives respectively.

In the time-exposure test, in which a bacterial suspension was mixed with the test sample and after 1, 5, and 10 minutes, the TM selective medium plates were inoculated from the mixture, only three contraceptives (Nos 4, 17, and 19) at 1 per cent. dilution inhibited the bacterial growth (Table III). Two

preparations (Nos 4 and 19) were effective in inhibiting the bacterial growth even after 1 minute exposure. Eight of the contraceptives were effective at 10 per cent. concentration, but some of these required 5 or 10 minutes contact to inhibit the bacterial growth.

By the plate-dilution method, in which dilutions of the test sample were incorporated into the TM selective medium, two preparations were effective at 1 per cent. concentration and eleven were effective at 10 per cent. dilution (approximately 1 per cent. final concentration in the growth medium). The pH of the medium was 7.2 ± 0.2 and did not change significantly after addition of the diluted test sample.

The time-exposure technique was found to be the more sensitive of these two methods. In most cases the contraceptive dilution which was effective by the time-exposure technique was also effective by the plate-dilution method. However, with the exception of two preparations (Nos 4 and 13), a low concentration of contraceptives was required for inhibiting the bacterial growth by the time-exposure method as compared to the plate dilution.

Several non-contraceptive preparations were also found effective (Table IV). Again, with the exception of some samples, the dilutions which were effective by time-exposure also inhibited growth by plate-

TABLE II Dilutions of non-contraceptives required to immobilize *T. pallidum* suspension within 1 to 1.5 minutes*

Group	Name of non-contraceptive	Concentration (per cent.)	No. of contraceptives	pH range
A	Neo-Silvol, Silver Protein, Vagisec Liquid Douche	1	3	6.8-9.4
B	Betadine Vaginal Gel, Candepin Vaginal Tablets, Emko Concentrate, Penigin, Penigin C, Sporostacin Vaginal Cream, Trib Vaginal Cream, Vabal D Base, Vabal D Cream	10	9	3.5-7.2
C	Koromex A Base only, Trimo San Vaginal Jelly	20	2	5.6-5.8
D	Progonasyl, Propion Gel	50	2	6.6-7.7
E	Iso-Sol Argryol	100	1	8.5

*Control from pH 3.5 to 9.4 did not immobilize spirochaetes in 5 minutes

TABLE III *Highest dilution of 20 contraceptives required to inhibit the growth of N. gonorrhoeae by two methods^a*

No.	Contraceptive	Time-exposure method					Plate-dilution method		
		Concentration (per cent.) ^b	pH	Growth after exposure (min.)			Concentration (per cent.)	pH ^c	Growth ^d
				1	5	10			
1	Certane Vaginal Jelly	10	4.6	+	-	-	10	7.5	-
2	Contra Creme	50	6.9	+	±	-	10	7.5	-
3	Contra Foam	10	7.5	±	-	-	10	7.5	-
4	Cooper Creme	1	6.7	-	-	-	10	7.6	-
5	Delfen Cream	20	5.2	+	+	+	10	7.6	-
6	Delfen Foam	50	4.9	-	-	-	20	7.6	-
7	Emko Concentrate	50	7.4	-	-	-	20	7.5	-
8	Emko Concentrate + A	50	7.1	-	-	-	20	7.2	-
9	Emko Concentrate + B	50	7.2	-	-	-	20	7.2	-
10	Emko Concentrate + Spermicide	20	7.0	+	+	-	20	7.3	-
11	Emko Foam	10	7.3	-	-	-	10	7.4	-
12	Immolin Vaginal	50	4.9	-	-	-	10	7.5	-
13	Koromex A Vaginal Jelly	10	6.0	+	-	-	50	7.5	-
14	Lanesta Gel	10	5.6	+	-	-	10	7.5	-
15	Lorophyn Suppositories	10	5.7	+	-	-	10	7.5	-
16	Milex Crescent	10	5.7	-	-	-	10	7.5	-
17	Ortho Creme	1	6.2	+	-	-	1	7.4	-
18	Ortho-Gynol Jelly	10	5.5	+	-	-	10	7.4	-
19	Preceptin Gel	1	5.6	-	-	-	1	7.4	-
20	Ramses Vaginal	50	6.7	+	+	-	50	7.5	-

^aBacterial suspension for these experiments contains about 10⁶ CFU per 0.1 ml., the inoculated Thayer-Martin selective medium plates were incubated at 37°C. in CO₂ incubator

^bOnly 50, 20, 10, and 1 per cent. dilutions in physiological saline solution were tested

^cpH of media after adding the contraceptive at different concentrations

^dResults from duplicate plates

TABLE IV *Highest dilution of 17 non-contraceptive preparations required to inhibit the growth of N. gonorrhoeae by two methods^a*

No.	Preparation	Time-exposure method					Plate-dilution method		
		Concentration ^b (per cent.)	pH	Growth after exposure (min.)			Concentration (per cent.)	pH ^c	Growth ^d
				1	5	10			
1	Betadine Vaginal Gel	10	3.7	-	-	-	20	7.6	-
2	Candepin Vaginal Tablets	50	6.9	+	+	+	50	7.6	+
3	Emko Concentrate No Active Ingredient	10	7.2	-	-	-	10	7.5	-
4	Iso-sol Argyrol	50	8.5	-	-	-	1	7.3	-
5	Koromex A Base only	50	5.3	+	+	+	50	7.6	-
6	Neo-Silvol	10	6.9	+	-	-	-	-	-
7	Penigin	1	4.6	+	-	-	1	7.6	-
8	Penigin C	1	4.5	-	-	-	1	7.4	-
9	Progonasyl	50	7.7	-	-	-	10	7.4	-
10	Propion Gel	50	6.6	+	-	±	50	7.0	+
11	Silver Protein	5	9.5	-	-	-	1	7.3	-
12	Sporostacin Vaginal Cream	50	3.0	±	-	-	10	7.3	-
13	Trib Vaginal Cream	50	5.3	±	-	-	20	7.4	-
14	Trimo San Vaginal Jelly	50	4.6	+	-	-	10	7.4	-
15	Vabal D Base	50	4.8	+	+	+	50	7.4	-
16	Vabal D Cream	20	5.7	+	-	-	10	7.5	-
17	Vagisec Liquid Douche	50	9.2	+	+	+	50	7.3	-

dilution. Only one preparation (No. 1) was found more effective by the time-exposure method.

The effect of exposure of *N. gonorrhoeae* to the different pH ranges encountered with contraceptive and noncontraceptive preparations was studied by adjusting the pH of physiological saline with 1N HCl or NaOH. The results are shown in Table V; the growth of gonococci was not inhibited by exposure for up to 10 minutes in acid or alkaline pH from 3.0 to 10.5. However, the test micro-organisms were not viable after exposure for more than 1 minute at pH 2.5.

TABLE V *Effect of pH on viability of Neisseria gonorrhoeae in physiological saline solution*

Sample No.	pH	Growth ^a after exposure (min.)		
		1	5	10
1	2.5	--	-	-
2	3.0	++	+	+
3	3.5	+	+	+
4	5.5	++	++	+
5	6.9	+	+	+
6	7.6	+	+	+
7	9.2	+	+	+
8	9.9	+	+	+
9	10.5	+	+	+
Control	6.8	+	+	+

^aBacterial suspension used for this study contains about 10⁸ CFU/0.1 ml. Inoculated Thayer-Martin selective medium plates incubated at 37°C. in CO₂ incubator

Discussion

The increase in incidence of venereal infection during recent years has created a challenge. Many of the control methods that are used routinely for other diseases are not easily adapted to venereal diseases. It is very evident that diseases of this nature cannot be reduced by effective therapy alone; prophylactic methods are necessary in addition for prevention and control.

With the foregoing in mind, and the fact that extensive testing, including some years of observation, is required for a new product to be approved for use in man by the Food and Drug Administration (FDA), it was considered desirable to attempt to find a product having the properties both of a contraceptive and of a prophylactic approved by the FDA in the very near future, so as to obviate long delays in placing effective products at the disposal of the public health programme. Contraceptive preparations for vaginal application are widely used and well accepted by many groups as effective birth control agents. It was thus decided to test these first for their effect on the two most frequently occurring venereal disease organisms, the gonococcus and *T. pallidum*.

The pathogenic treponemata are very delicate

micro-organisms and require a special micro-environment for survival. Any preparation with spermicidal activity might be expected to have spirochaeticidal effect, and the results reported in this study indicate that many contraceptives available in the market have spirochaeticidal effect to various degrees, at least as judged by immobilization of the micro-organisms *in vitro*. Many non-contraceptive preparations also showed spirochaeticidal properties by this criterion.

Whether these immobilized treponemes are still infectious or not, can only be answered by studies *in vivo*. The studies *in vitro* reported here may not simulate the situation *in vivo*, but it is possible to compare the relative effectiveness of various test samples for their effect on motility. Testing *in vitro* is a fast and, within limits, a reliable method for screening a large number of test samples. It is planned that the selected preparations will be tested *in vivo* on rabbits. Similar techniques were used in the study of the prophylaxis of syphilis and were eventually accepted in the development of a highly effective preparation, Orvus-Mapharsen solution, to prevent syphilis (Arnold and Cutler, 1956; Arnold and Mahoney, 1948).

Unfortunately there is no readily available animal model for conducting such experiments to study gonococcal infection. However, two types of tests to determine bactericidal or bacteriostatic effects as reported in this study can be used to select the preparations which are more effective for inhibiting the growth of *N. gonorrhoeae* and which may then be considered for clinic study. The concentrations of various preparations which effectively inhibit the growth of *N. gonorrhoeae* as found by such studies are relative values and should by no means be considered the absolute effective value of these products. Nevertheless, under similar experimental conditions, the results are reproducible and were used to compare minimum inhibitory concentration (MIC) and or minimum lethal concentration (MLC) of these contraceptive and non-contraceptive preparations. The preparations which were effective by the time-exposure techniques were also effective by the plate dilution method. The differences in effective concentration by the two types of tests are due to various factors such as solubility, compatibility, stability, thermo-lability, the pH of the medium, and the bacteriostatic or bactericidal properties of the test samples.

The exposure to changes in pH alone in the range of 3.0 to 10.5 up to 10 minutes before streaking was not found to inhibit the growth of gonococci. The role of the pH in the viability of gonococci will be studied further by more quantitative techniques.

Recent studies showed that the commonest causes of vaginal discharges were *Trichomonas vaginalis* and *Candida albicans* (Catterall, 1970). The possible implication of these and other sexually transmissible diseases in regard to pregnancy, fertility, or the development of cervical cancer should be considered (Willcox, 1970). The role of immunization as a possible method to prevent such sexually transmitted diseases is under study. However, local chemical or drug prophylaxis might well be found effective in preventing the transmission of certain of these and other genital infections as well as of the common venereal diseases.

It is postulated that a product which simultaneously prevented both conception and a wide variety of different genital infections would be a most valuable adjunct to the existing Public Health measures. It would fit into the family planning and V.D. control programmes existing in most national health services. These preliminary studies are encouraging, and further work along these lines is in progress.

Summary

Twenty vaginal contraceptive preparations and seventeen other compounds, mostly vaginal antiseptics, were studied *in vitro* for their effect on the motility of virulent *T. pallidum* and were also tested for their bactericidal or bacteriostatic effects on *Neisseria gonorrhoea*. Concentrations of several contraceptives and other preparations as low as 1 per cent. were effective in immobilizing spirochaetes in suspension within 1 to 1.5 minutes. Similarly, several products inhibited gonococcal growth as shown by time-exposure as well as plate-dilution techniques. These results *in vitro* are reported. Further studies *in vitro* and *in vivo* are in progress to find the preparations which show the greatest potential for topical use in V.D. prophylaxis and contraception.

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Sur une préparation vaginale assurant à la fois la prophylaxie des maladies vénériennes et des autres infections génitales et la contraception II. Effet *in vitro* de préparations vaginales contraceptives et non contraceptives sur *Treponema pallidum* et *Neisseria gonorrhoeae*

SOMMAIRE

Vingt préparations vaginales contraceptives et dix-sept autres composés, principalement des antiseptiques vaginaux, ont été étudiés *in vitro* sur la mobilité du *T. pallidum* virulent et éprouvés aussi pour leur effet bactéricide ou bactériostatique sur *Neisseria gonorrhoeae*. A des concentrations aussi faibles que 1 pour cent, plusieurs contraceptifs et d'autres préparations immobilisèrent les spirochètes en suspension en 1 à 1,5 minute. De même, plusieurs produits inhibèrent la pousse du gonocoque, comme ceci fut montré par la durée de contact nécessaire ou la technique des dilutions sur plaques. Ces résultats *in vitro* sont rapportés. Des études ultérieures, *in vitro* et *in vivo*, sont en cours pour trouver les préparations se montrant les plus puissantes en emploi local pour la prévention des maladies vénériennes et la contraception.

APPENDIX

Names and Sources of Contraceptive and Non-contraceptive Preparations Tested

<i>Preparations tested</i>	<i>Company</i>
CONTRACEPTIVES	
Certane Vaginal Jelly	Vogarell Products Co. 1212 W. Washington Blvd, Los Angeles, California
Contra Creme	Research Supplies, Pine Station Box 8025, Albany, New York 12203
Contra Foam	Contra-Foam Inc. Flushing, New York
Cooper Creme	Whittaker Laboratories Inc. Peekskill, New York 10566
Delfen Cream	Ortho Pharmaceutical Corp.
Delfen Foam	Raritan, New Jersey 08869
Emko Concentrate	Emko Company
Emko Concentrate + A	7912 Manchester Ave., St. Louis, Missouri 63143
Emko Concentrate + B	
Emko Concentrate + Spermicide	
Emko Foam	
Immolin Vaginal Cream-Jel	Julius Schmid Inc. 423 West 55th St., New York, N.Y. 10019
Koromex A Vaginal Jelly	Holland Rantos Co. Enterprise Ave., Trenton, N.J. 08683
Lanesta Gel	Esta Medical Laboratories Inc. Alliance, Ohio
Lorophyn Suppositories	Eaton Laboratories Division of Norwich Pharmacology Co. Norwich, New York 13815
Milex Crescent Jelly	Milex Products 5915 Northwest Highway, Chicago, Illinois 60631
Ortho Creme	Ortho Pharmaceutical Corp.
Ortho Gynol Jelly	Raritan, N.J. 08869
Preceptin Gel	Ortho Pharmaceutical Corp. Raritan, N.J. 08869
Ramses Vaginal Jelly	Julius Schmid Inc. 423 West 55th St., New York, N.Y. 10019
NON-CONTRACEPTIVES	
Betadine Vaginal Gel	Purdue Frederick Co. 99 Saw Mill River Road, Yonkers, New York 10701
Candeptin Vaginal Tablets	Julius Schmid Inc. 423 West 55th St., New York, N.Y. 10019
Emko Concentrate (no active ingredient)	Emko Company 7912 Manchester Ave., St. Louis, Missouri 63143
Iso-sol-Argyrol	Tilden Yates Laboratories Fairfield Road, Wayne, New Jersey 07470
Koromex A (base only)	Holland Rantos Co. Enterprise Ave., Trenton, N.J. 08683
Neo-Silvol	Parke Davis & Co. Detroit, Michigan 48232
Penigin	Sankyo Co. Ltd.
Penigin C	Tokyo, Japan
Progonasyl	American Pharmacology Laboratories Inc. San Antonio, Texas 78209
Propion-Gel	Wyeth Laboratories Inc. P.O. Box 8299, Philadelphia, Pa. 19101
Silver Protein	Mallinckrodt Chemical Works St. Louis, Mo.

<i>Preparations tested</i>	<i>Company</i>
Sporostacin Vaginal Cream	Ortho Pharmaceutical Corp. Raritan, N.J. 08869
Trib Vaginal Cream	Roche Laboratories Division of Hoffman La Roche Inc. Nutley, N.J. 07110
Trimo San Vaginal Jelly	Milex Products 5915 Northwest Highway, Chicago, Ill. 60631
Vabal D Base	Semed Pharmaceuticals Division of S.E. Massengill Co. Bristol, Tenn. 37620
Vagisec Liquid Douche	Julius Schmid Inc. 423 West 55th St., New York, N.Y. 10019
