of the ground glass joint to the Dreschel gas drying apparatus containing 30 cc. of 20% potassium iodide solution. Keep the receiver cold in a beaker of circulating water. Add an excess of ferric chloride (about 5 Gm.) to the retort and gently heat to boiling. Continue the distillation for about 30 min. in such manner as to cause the gases to bubble continuously into the potassium iodide solution. Disconnect the apparatus at the ground glass joint, wash the delivery tube with water and titrate the liberated iodine with 0.1 *N* sodium thiosulfate solution using starch indicator.

The accuracy of the method is evidenced by recoveries of iodine recorded in Table III.

Table III.—Recoveries of Iodine

Detn.	Iodine Weighed	Iodine Recovered	Per Cent Recovery
1	0.3937	0.3914	99.42
2	0.2814	0.2813	99.96
3	0.4483	0.4480	99.93
4	0.3169	0.3162	99.78
5	0.3916	0.3905	99.72
6	0.4396	0.4393	99.93
7	0.3608	0.3589	99.61
8	0.3627	0.3615	99.67
9	0.4408	0.4406	99.95
10	0.3449	0.3448	99.97
11	0.4379	0.4383	100.09
		Average	99.82

Blank determinations were made using the same procedure but with omission of the iodine. Results showed that the vapors from the flask had very little or no reducing action upon the potassium iodide in the receiver. Other experiments were made showing that gelatin (commonly used as pill coating) did not decrease the efficiency of the method.

Table IV.—Analysis of Commercial Brands of Pills of Ferrous Iodide

Company	No. of Detns.	Labeled FeI_2, Gm. per 2 Pills	Determined FeI_2, Gm. per 2 Pills
P. D. & Co.	3	0.122	0.125
Foreign	3	0.09	0.10
Upjohn	3	0.067	0.065

The procedure was applied to analysis of commercial brands of ferrous iodide pills and gave results recorded in Table IV.

SUMMARY

The efficiency of methods proposed in the literature for determining iodide content of mixtures was determined by applying the procedures to analysis of quantitatively prepared mass of ferrous iodide. None of the methods gave accurate or consistent recoveries of iodine.

Kolthoff's method was modified to give satisfactory recoveries of iodine, but the procedure was time-consuming.

A method for the determination of iodide in the presence of interfering substances has been developed by the authors. It is based on the release of iodine with ferric chloride in a specially designed distillation apparatus. The procedure proved to be convenient and it gave accurate recoveries of iodine from samples of quantitatively prepared mass of ferrous iodide.

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A Study of Antiseptics in Various Ointment Bases*

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As early as 1881 Koch observed that phenol, when dissolved in oil or alcohol, showed less bactericidal action than it did in aqueous solution. In 1895 Breslauer (1) reported upon the bactericidal effects of ointments, and concluded that cold cream and lanolin were the best ointment bases for antiseptics. A few years later Eldred (2) showed the presence of bacteria or molds in thirty of the fifty samples of official ointments and bases which he tested.

* Submitted to the faculty of Purdue University in partial fulfillment of the requirements for the degree of Master of Science, 1941.

Presented to the Scientific Section of the A. PH. A., Detroit meeting, 1941.

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In 1929 Reddish and Wales (3) tested 12 ointments of the U. S. Pharmacopœia and 14 of the National Formulary, and found that only five of the former and six of the latter ointments exhibited antiseptic properties. They found that calamine ointment which contained 17% zinc oxide in a base composed chiefly of lard was antiseptic, but that zinc oxide ointment, 20%, in a paraffin and petrolatum base showed no antiseptic action. They concluded that because of the influence exerted by the base it was impossible to predict the antiseptic action of an ointment from the antiseptic value of its constituents.

Rose (4) showed that ointments of ammoniated mercury, iodine, thymol iodide, yellow oxide of mercury, mercury, 30%, and calomel were bacteriostatic, while those of sulfur, zinc oxide, compound resorcinol, ichthyol and tar were not.

Gershenfeld and Miller (5) found that self-emulsifying wax and water-miscible vanishing cream bases were satisfactory vehicles for antiseptics. At about the same time Craw and Lee (6) showed that ointment of phenol, 2%, was not bacteriostatic in a variety of bases, but that the halogen derivatives of *o*-phenylphenol in concentrations as low as 1%, in the same bases, had a marked bacteriostatic action. They concluded that the antiseptic action of ointments is dependent quite as much upon the nature of the chemical as upon the composition of the base.

Prout (7) and his co-workers prepared a series of antiseptic ointments using silica gel as the base. He stated that "there are significant differences, between the individual antiseptic medicaments, which would be expected inasmuch as the germicidal power of the medicaments *per se* varies greatly."

Gershenfeld (8) has proposed the following classification of ointment base groups, according to the size of the zone of inhibition, upon being tested in the usual manner: (*a*) synthetic wax base, (*b*) oxycholesterin base, (*c*) benzoinated lard, (*d*) U. S. P. XI ointment, and (*e*) petrolatum base. Fiero (9) has shown that a partially hydrogenated oil base is superior to the official ointment base for ointment of ammoniated mercury.

EXPERIMENTAL

This investigation has been made for the purpose of studying the antiseptic action of various commonly known chemicals in bases of various types: fatty, non-fatty, water-absorption and gels.

Staphylococcus aureus was the test organism used in this study. The U. S. Department of Agriculture Agar-Plate and Agar-Cup-Plate methods were used, as outlined in Circular No. 198.

Inasmuch as there has been some discussion over the efficacy of wool fat-petrolatum-wax mixtures, in varying proportions, as bases for antispetic ointments a series of such were tested with phenol, 2%, and ammoniated mercury, 10%. Table I shows the

Table I

	Base			Antiseptic Action	
No.	Hydrous Wool Fat, Gm.	White Petrolatum, Gm.	White Wax, Gm.	Ammoniated Mercury, 10%	Phenol, 2%
1	10	90	0	6[a]	..
2	20	80	0	6	..
3	30	70	0	6	..
4	40	60	0	6	..
5	50	50	0	6	..
6	60	40	0	6	..
7	70	30	0	6	..
8	80	20	0	6	..
9	90	10	0	6	..
10	10	85	5	6	..
11	20	75	5	6	..
12	30	65	5	6	..
13	40	55	5	5	..
14	50	45	5	6	..
15	60	35	5	5	..
16	70	25	5	5	..
17	80	15	5	5	..
18	90	5	5	5	..

[a] Zones of inhibition in mm. The average of three or more plates.

ointment formulas and the results of the antiseptic tests. The 2% phenol ointments were consistently not bacteriostatic. The results are shown here merely to contrast them with the positive results of the ammoniated mercury formulas.

A second series of 18 formulas was prepared substituting anhydrous wool fat for the hydrous product. Similar antiseptic tests were made with comparable results except that the zones of inhibition averaged about 1 mm. less for the ammoniated mercury ointments. It is possible that this variation may be attributed to the difference in the water content of the two wool fats. The phenol ointments showed no such variation.

WATER HOLDING BASES

A number of workers have proposed several so-called water holding bases as vehicles for antiseptic ointments. It has been stated that bases of this type are more compatible with the skin, especially

Table II

Base or Ointment	Ointments, Official Strength: Boric Acid Mm.[a]	Ammoniated Mercury, Mm.	Yellow Oxide Mercury, Mm.	Calomel, Mm.	Phenol, Mm.	Iodine, Mm.	Whitfield's, Mm.	Ichthamol, Mm.	Calamine, Mm.	Zinc Oxide, Mm.
U. S. P. ointment	..[b]	6	5	0	..	10	0	0	0	..
N. F. ointment	0[c]	0	0	3	0	0	4	3	3	..
Petrolatum	..	5	5	1	..	10	4	3	..	..
Hydrous wool fat	..	7	5	3	..	15	6	3	1	..
Anhydrous wool fat	..	6	4	3	..	14	6	2	..	..
Aquaphor	..	6	5	1	..	20	4	0	..	..
Aquaphor-Water *aa*	4	6	5	3	..	*I*[d]	7*I*	4	..	..
Base 37	..	6	5	1	..	15	4	0	3	..
Base 37-Water *aa*	4	6	5	3	..	*I*	7	4	5	..
Neutramul	0	6	6	0	..	*I*	0	0	0	..
Neutramul-Water *aa*	0	6	6	0	0	*I*	0	0	0	..
Gardinol Base	0	6	0	0	..	0	0	0	0	..
133 T (Goldschmidt Corp.)	0	0	5	0	1	0	0	4	..	..
Seltzer Base 4-Water *aa*	0	0	0	0	4	0	0	0	0	..
Vanishing cream[e]	5	10	8	4	3	*I*	7	4	2	2
Sodium alginate, 5%[e]	9	0	8	4	2	*I*	*I*	*I*	2	2
Methyl cellulose 1500, 5%[e]	9	6	8	4	0	*I*	*I*	*I*	2	2
Methyl cellulose 1500, 15%[e]	0	6	0	3	3	*I*	0	*I*	0	0

[a] Width of zones of inhibition in millimeters.
[b] Negative results.
[c] No test made.
[d] Incompatibility.
[e] Controls showed zones of inhibition of 1 to 2 mm.

so with irritated or exposed areas, and permit more prompt and thorough diffusion of the antiseptic medicament from the base to the affected part.

It is not possible to duplicate conditions *in vitro* as they may be found *in vivo* but certain comparisons can be made. In Table II the zones of inhibition of eight commonly accepted antiseptics in ointment form are shown. Ointments of calamine and of zinc oxide are also shown. The latter gave essentially negative results, but is reported by way of contrast with calamine.

The formulas for several of the proposed new type bases need to be given in order to get a comparison of their value as vehicles for antiseptic ointments. Base 37, proposed by Johnston and Lee (10), is as follows:

Cholesterol	5 Gm.
Anhydrous wool fat	20 Gm.
Liquid petrolatum	45 Gm.
Cetaceum	25 Gm.
White wax	5 Gm.

Seltzer (11) has proposed the following formula for Neutramul:

Sodium lauryl sulfate	2 Gm.
Cetyl alcohol	12 Gm.
Stearyl alcohol	6 Gm.
Ceresin, white	5 Gm.
Liquid petrolatum, heavy	45 Gm.

Burnside and Kuever (12) offer the following formula for Gardinol Ointment Base:

Gardinol	0.25 Gm.
Propylene glycol	6.00 Gm.
Water	1.92 Gm.
White petrolatum	91.83 Gm.

The Goldschmidt Corporation (13) suggests the following formula for an all-purpose cream:

Tego stearate	4.0 Gm.
Beeswax	9.0 Gm.
Water	49.0 Gm.
Borax	1.2 Gm.
Paraffin	12.0 Gm.
Mineral oil	20.0 Gm.
Petrolatum	4.0 Gm.

Another formula in this series is the one which Seltzer designates as Base 4. It is as follows:

Sodium lauryl sulfate	2.0 Gm.
Cetyl alcohol	12.0 Gm.
Stearyl alcohol	3.0 Gm.
Oleyl alcohol	3.0 Gm.
Ceresin, white	5.0 Gm.
Liquid petrolatum, heavy	45.0 Gm.

The vanishing cream formula used is as follows:

Stearic acid	32.00 Gm.
Oil peach kernel	24.00 Gm.
Cetaceum	4.00 Gm.
Glycerin	9.00 Gm.
Ammonia water	4.44 ml.
Hot water	148.00 ml.
Bay rum	25.00 ml.
Oil orange flowers	.50 ml.
Oil lavender	.10 ml.

The methyl cellulose, 5% and 15%, and the sodium alginate, 5%, were gel-like products to which the medicinal agent was added. These were tested because of the interest which has been shown in substances which might serve as non-fatty ointment bases.

SUMMARY AND CONCLUSIONS

Boric acid was negatively bacteriostatic in the fat-like bases but positive in the hydrophilic compounds in which large amounts of water were present.

Ammoniated mercury was consistently active in all of the bases, but most active in vanishing cream, and slightly more active in hydrous wool fat than in the anhydrous fat.

Yellow oxide of mercury gave positive reactions in all the bases used, with the largest zones of inhibition in vanishing cream, sodium alginate and methyl cellulose. Since the controls for these three bases gave zones of inhibition of 1 to 2 mm., the increased zones with them are not particularly significant.

Calomel was, in general, more active in the hydrophilic bases but equally active in anhydrous wool fat.

Phenol was inactive in the usual bases, showing most activity in the Seltzer Base 4 with an equal amount of water, and with vanishing cream, sodium alginate, and methyl cellulose, 15%. Discounting the activity of the controls of the three latter products, the results are not very significant.

Iodine, the most active antiseptically of all the chemicals, behaved very well in all of the fat-like bases. It was incompatible with Neutramul and those vehicles containing large amounts of water.

Whitfield's Ointment was more active in the water-holding bases, but in the most highly aqueous ones developed incompatibilities upon standing. Ichthammol behaved in about the same way, but a little less so.

The inactivity of zinc oxide in all of the ordinary bases was quite in keeping with our past experience. The small zones of inhibition shown with vanishing cream, sodium alginate and methyl cellulose are not significant. The activity of calamine, erratic as it was, is puzzling.

At first glance the results of this study would seem to present a good case in favor of the water-holding bases as vehicles for the antiseptic chemicals. Upon closer examination it will be observed that ammoniated mercury, yellow oxide of mercury, calomel, iodine, benzoic and salicylic acids, ichthammol and even prepared calamine were all bacteriostatic as official ointments. The antiseptic action of each was not greatly accelerated when incorporated in the water-holding bases such as Aquaphor, Base 37, Neutramul, and similar products.

The results with boric acid in the highly hydrated water-holding bases are interesting and perhaps deserving of further study.

It may be said that the presence of water in some of the bases seemed to increase the diffusion of the chemicals into the agar, resulting in larger zones of inhibition. The results were not consistent, however, for all of the chemicals tested.

Therefore, in general, it may be concluded from the results of these experiments that the nature of the chemical or medicament which is incorporated in a base has as much or perhaps more to do with the bacteriostatic action of the product than does the composition of the vehicle in which it has been incorporated.

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