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SUBJECTS.

- Study of the Germination of Belladonna Seeds.
- Study of the Planting of Belladonna.
- Effect of Fertilization upon the Growth of Belladonna Plants.
- Effect of Moisture upon the Growth of Belladonna Plants.
- Effect of Shade upon the Growth and Development of Belladonna Plants.
- Study of the Means of Combating Insects on Belladonna Plants.
- Study of the Effect of Drying Belladonna Leaves at Different Temperatures upon the Alkaloid Content.
- Study of the Production of Seeds by Belladonna Plants.
- Influence of the Presence of Stems upon the Alkaloid Content of Belladonna Leaves.
- Summary.
- Bibliography.

A STUDY OF VARIOUS PNEUMOCOCCIDAL SOLUTIONS FOR MOUTH WASHES.*

BY S. SOLIS COHEN, M.D., AND EDWARD STEINFELD, M.D.

Dochez and Avery,¹ Stillman² and Sydenstricker and Sutton³ have demonstrated that infection in pneumonia occurs by way of the upper respiratory tract, through contact with pneumonia patients, convalescents or carriers, harboring virulent fixed strains of pneumococci in the mouth.

At the request of one of us (S. S. C.) Kolmer and Steinfield⁴ investigated the use of specific pneumococcidal substances such as ethylhydrocuprein hydrochloride, quinine and urea hydrochloride, quinine bisulphate and other cinchonics incorporated in a mouth wash. They found that ethylhydrocuprein was effective as a pneumococcicide in solution so dilute as 1 : 160,000, and the quinine salts in solutions of about 1 : 20,000. The strongest solution they could induce patients to use was 1 : 10,000. They recommend, accordingly, the use of quinine hydrochloride 1 : 10,000 in the "Liquor Thymolis" of the House Pharmacopeia of the Philadelphia Polyclinic, as a means of diminishing the chances of infection in nurses and physicians and minimizing the dangers of spread by carriers. In their experiments, however, this solution could not keep the mouth and throat secretions continuously sterile.

* From the Clinical Laboratories of the Jewish Hospital, Philadelphia.

It seemed probable that the use of the cinchonics in greater concentration might prove more uniformly effective under varied conditions; but to make this practicable the solutions must be rendered palatable, or, at least, not unpalatable.

To test this, a number of solutions were made up for us by Professor E. Fullerton Cook, with various flavoring vehicles. They contained quinine and urea hydrochloride—chosen because of its high solubility—in various strengths up to as high as $\frac{1}{2}$ and 1 percent, in which it develops anesthetic power. Some contained phenol in addition to the quinine. Honey, syrup, glycerin or acacia was used to give the mixture an adhesive quality that would retain it in contact with the mucous membranes for some time after rinsing or gargling.

These mixtures were tested by cultural methods both upon pure cultures of Type I, II and III pneumococcus, and upon sputum containing virulent pneumococci.

The method of study was as follows:

In a series of sterile test-tubes were placed 0.5 Cc. of a cinchonic solution and 0.5 Cc. of a suitable dilution of pneumococcus culture (usually 1 : 2) or 0.5 of sputum of a pneumonia patient. These were mixed and incubated at 37.5° C. for one-half hour. At the expiration of this period a platinum loopful from each tube was plated into 10 Cc. of glucose agar or blood agar. The virulence of the cultures used was such that 0.000001 Cc. was fatal to white mice in from 24 to 48 hours after intraperitoneal injection.

Two points were to be determined: 1. Do the vehicles used for palatability interfere with the quinine action? 2. Do these vehicles enhance the effect—in other words, have they germicidal qualities of their own?

In the tables giving the results of the experiments the various solutions are represented by the numerals which designate them in the following list (with brief parenthetic memoranda):

FORMULAS OF SOLUTIONS USED.

No. 1.		No. 6.	
Vehicle Control—5% Infusion of Coca.		Quinine and Urea Hydrochloride.....	1
		Compound Gargle of Guaiac to make..	100
No. 2.		No. 7.	
Quinine and Urea Hydrochloride.....	1	Quinine and Urea Hydrochloride.....	1
Infusion of Coca.....	100	Acacia.....	10
No. 3.		Compound Gargle of Guaiac to make..	100
COMPOUND GARGLE OF GUAIAIC (N. F.).		No. 8.	
Ammoniated Tincture of Guaiac.....	100	Quinine and Urea Hydrochloride.....	1
Compound Tincture of Cinchona.....	100	Acacia.....	5
Clarified Honey.....	200	Compound Gargle of Guaiac to make..	100
Potassium Chlorate.....	40		
Oil of Peppermint.....	2	No. 9.	
Water to make.....	1000	Compound Gargle of Guaiac, with sub-	
No. 4.		stitution of Quinine and Urea Hydro-	
Compound Gargle of Guaiac with Coca—		chloride.....	10
Replace water of N. F. with 5% Infusion of		Water to make.....	100
Coca.		—for the 100 mls of Compound Tinc-	
No. 5.		ture of Cinchona	
Quinine and Urea Hydrochloride.....	1		
Compound Gargle of Guaiac to make	1000		

No. 10.		No. 13.	
Quinine and Urea Hydrochloride.....	0.5	Quinine and Urea Hydrochloride.....	1
Phenol.....	0.5	Phenol.....	1
Glycerin.....	20.0	Oil of Peppermint.....	2 drops
Oil of Peppermint.....	2 drops	Water.....	100
Water to make.....	100.0		
No. 11.		No. 14.	
Quinine and Urea Hydrochloride.....	1	Quinine Phenolate.....	1
Phenol.....	1	Menthol.....	1
Acacia.....	1	Expressed Oil of Almond.....	100
Compound Gargle of Guaiac.....	100		
No. 12.		No. 15.	
Quinine and Urea Hydrochloride.....	0.5	Phenol 1% (Control.)	
Phenol.....	0.5		
Syrup of Tolu.....	20.0	No. 16.	
Water to make.....	100.0	Quinine and Urea Hydrochloride 1% (Control.)	

TABLE I.—RESULTS OF BACTERICIDAL TESTS UPON TYPES I AND II PNEUMOCOCCUS CULTURES AND UPON SPUTUM OF A TYPE II PNEUMONIA.

No.	Formula.	—Colonies per Plate after 48 hours.—		
		Type I.	Type II.	Sputum, Type II.
1.	Infusion Coca.....	810	480	3,660
2.	Infusion Coca with 1 percent Quinine and Urea Hydrochloride.....	3	5	10
3.	Compound Gargle of Guaiac.....	17	25	182
4.	Compound Gargle of Guaiac with Infusion of Coca.....	21	71	1,260
5.	Compound Gargle of Guaiac with 0.1 percent Quinine and Urea Hydrochloride.....	22	9	31
6.	Compound Gargle of Guaiac with 1 percent Quinine and Urea Hydrochloride.....	3	Sterile	Sterile
7.	Same as No. 6 with 10 percent Acacia.....	16	51	720
8.	Same as No. 6 with 5 percent Acacia.....	8	81	8
9.	Compound Gargle of Guaiac with 1 percent Quinine and Urea Hydrochloride—Replacing Compound Tincture of Cinchona.....	Sterile	Sterile	Sterile
10.	Quinine and Urea Hydrochloride and Phenol each 1/2 percent, Glycerin, Oil of Peppermint and Water.....	Sterile	Sterile	Sterile
11.	Acacia, Phenol and Quinine and Urea Hydrochloride each 1 percent in Compound Gargle of Guaiac.....	Sterile	Sterile	Sterile
12.	Phenol and Quinine and Urea Hydrochloride each 1/2 percent in Syrup of Tolu and Water...	Sterile	Sterile	Sterile
13.	Phenol and Quinine and Urea Hydrochloride each 1 percent in Peppermint Water.....	Sterile	Sterile	Sterile
14.	Quinine phenolate and Menthol each 1 percent in Expressed Oil of Almond.....	Sterile	Sterile	Sterile
15.	Phenol 1 percent.....	Sterile	Sterile	Sterile
16.	Quinine and Urea Hydrochloride 1 percent.....	Sterile	Sterile	Sterile
	Control (Sputum and Salt Solution).....	1,150	540	4,860

The results as indicated in Table I showed but little interference of the vehicles with the germicidal action of the quinine except in those solutions containing acacia. In such solutions a constant and definite lessening of activity was ob-

served, which may possibly be due to a mechanical action. Mixtures made with Infusion of Coca are more palatable than those made with plain water, but show slightly lessened germicidal power and some precipitation of the quinine. Solution No. 10 (phenol, quinine and urea hydrochloride, glycerin, oil of peppermint and water) was chosen as being on the whole most palatable of those made without coca. This solution with other controls was therefore used against Type III pneumococci. The results of these tests are shown in Table 2.

TABLE 2.—RESULTS OF BACTERICIDAL TESTS UPON TYPE III PNEUMOCOCCI,—WITH SOLUTION NO. 10 AND VARIOUS COMPARISONS.

Solution.	Colonies per plate after 48 hours.
10.....	Sterile
Quinine Hydrobromide.....	Sterile
1 : 200	
Quinine Bisulphate.....	Sterile
1 : 200	
Ethylhydrocuprein Hydrochloride.....	Sterile
1 : 200	
Control.....	6,280

The results recorded in Table 2 showed that the same activity was noted against Type III as against the other types.

SUMMARY.

These experiments show that cinchonic solutions of high concentration may be made up with various vehicles of even thick consistency without materially altering the bactericidal power. The solution marked No. 10 is, however, water clear with no tendency to produce precipitates or sediments. Phenol has been included as a good reinforcing agent and suitable for its effects upon other pathogenic organisms such as streptococci. This is desirable in view of recent observations upon atypical pneumonias believed by Cole and McCallum⁵ to be due to hemolytic streptococci invading respiratory tracts of susceptible individuals such as patients suffering from measles.

CONCLUSIONS.

1. A number of quinine solutions in different flavoring vehicles have been made up with the purpose of determining palatability and germicidal activity against pneumococci.
2. These solutions have all been found capable of destroying pneumococci of Types I and II *in vitro*. Those containing acacia have been less efficacious than others. Neither glycerin, syrup nor honey seems to interfere materially with the action of the germicide.
3. A solution containing quinine and urea hydrochloride and phenol, each in a dilution of 1 : 200, made up with 20 percent of glycerin and flavored with oil of peppermint, is fairly palatable. This was tested against Type III pneumococci also and found effective. It exhibits, likewise, penetrative ability in sputum.
4. The solution mentioned in paragraph 3 may readily be associated with the compound guaiac gargle which has been found so effective against tonsillitis and other throat infections, and which of itself shows considerable germicidal ac-

tivity against pneumococci. To do this one simply substitutes compound gargle of guaiac (N. F.) for the water of formula No. 10.*

5. Infusion of coca may be substituted for water in all the formulas with advantage as to palatability, but owing to the tannin it contains, it precipitates some of the quinine. This may, perhaps, lessen slightly the germicidal activity, but it has been shown elsewhere⁶ that even insoluble quinine tannate in small proportions will inhibit the growth of pneumococci in test-tube cultures.

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A PLEA FOR A CLOSER STUDY OF PHARMACEUTICAL PREPARATIONS
IN THE LIGHT OF THE CRITICISMS OF THE MEDICAL
PROFESSION.†

BY L. E. SAYRE.

In the Epitome of the U. S. P. and N. F., published by the American Medical Association, these words occur in the introduction: "Both the Pharmacopoeia and the National Formulary include many drugs and preparations which are irrational, superfluous or worthless."

As these works are supposed to be largely the creation of the medical and pharmaceutical professions it has occurred to the writer that special coöperative effort might lead to some constructive scheme of elimination and possibly to a better feeling and understanding as to: Where lies the responsibility for these drugs and preparations—who stands sponsor for them and why? As it is, a small, uninformed number of the medical profession believes that pharmacists are responsible for the so-called irrational preparations, and some members of the pharmaceutical profession believe that they were brought into existence principally by physicians. Neither view is tenable. As a member of the Committee on Miscellaneous Formulæ I have never considered it my province to pass judgment on the therapeutical merit of any preparation, but to prepare a pharmaceutical product of the indicated ingredients. The same attitude has been taken with formulas sent to the laboratory by individual physicians, merely extracting the

* Clinically I have obtained excellent results by simply adding phenol, menthol, and quinine and urea hydrochloride, each one grain to the fluidounce (1 : 500) and glycerin one fluidrachm to the fluidounce (1 : 8) to the guaiac gargle. This, however, can be bettered by getting rid of the tannin, which tends to precipitate some of the quinine. As a general disinfectant for all pathogenic organisms the addition of formaldehyde solution, 1 drop to the ounce, improves it further and the taste is not made worse.—S. S. C.

† Read before Section on Practical Pharmacy and Dispensing, A. Ph. A., Chicago meeting, 1918.