NOTES ON ANTISEPTIC SOLUTION—NATIONAL FORMULARY.*

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In the manufacture of antiseptic solution of the National Formulary, much of the expensive, active ingredients is removed by filtration because of the lack of solubility under these conditions. An approximation indicates that possibly as much as eighty per cent of these valuable ingredients is removed by filtration.

Apparently the revision committee of the National Formulary is aware of difficulties in this preparation because the formula for antiseptic solution is different in each of the last three National Formularies. It appears that the omission of sodium benzoate and sodium salicylate in N. F. V left something to be desired in antiseptic properties for N. F. VI has included chlorthymol, a germicide which has six times the germicidal activity of thymol. This inclusion would make an ideal preparation from a germicidal standpoint, if the chlorthymol were all dissolved. This, however, does not happen; for if the solution is filtered brilliantly clear before the addition of chlorthymol and then chlorthymol is added, oily drops separate.

Possibly the omission of sodium benzoate and sodium salicylate was made with the object of reducing the tendency of this solution to color and also to improve the taste. The coloration was very slight and as far as the taste is concerned the flavoring ingredients completely hide any sweetish saline taste that these salts impart. Two very valuable properties are lost by this omission; one is the loss of the antiseptic power of these two salts and any synergestic action which these salts may have, the other is the surface tension lowering produced by these salts.

The following facts indicate that antiseptic solution of the National Formulary VI does not contain all of the valuable constituents used in the formula.

1. It requires approximately four and one-half times the official volume of alcohol 30, water 70 to completely dissolve all the constituents.

2. The solution as prepared in 1 compares favorably in germicidal power with the official antiseptic solution.

3. On chilling the official solution and the solution described in 1 both become cloudy within 1° C. of the other. The official solution clouds about 1° C. higher than the dilution.

4. Thymol and chlorthymol are very soluble in the other aromatic and oily constituents; therefore the oily residue which is present before filtration must dissolve most of the thymol and chlorthymol. A coarse approximation indicates that more than three-fourths of these active materials are lost.

5. Theoretically chlorthymol with a phenol coefficient of 120 and thymol with a phenol coefficient of 20 should make a solution equal to a 14 per cent solution of phenol if all of these substances are present.

Chlorthymol	0.1 Gm. × 120 =	12.0 Gm. phenol
Thymol	0.1 Gm. × 20 =	2.0 Gm. phenol
		14.0 Gm. Phenol in 100 cc.

A three per cent solution of phenol is recognized as an effective germicide and therefore if all of the valuable constituents are present in the official antiseptic solution 14/3 or one part of antiseptic solution diluted with about 3.6 parts of water

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to make 4.6 parts of solution should be an effective germicide. However, the National Formulary directs that the official antiseptic solution be used undiluted, because if it is diluted appreciably it loses its germicidal power for the lack of germicide.

When tested bacteriologically a 1:1000 solution of thymol kills *Staphylococcus aureus* of prescribed resistance when tested at 37° C. within five minutes, using the Food and Drug Administration Phenol Coefficient Method. Chlorthymol has six times the phenol coefficient of thymol; hence a 1:6000 solution of chlorthymol should be equal to a 1:1000 thymol, or a dilution of one part of antiseptic solution N. F. VI in water to make seven parts should kill, but it does not kill because all the germicidal substances are not present. Nevertheless, when all the germicidal substances are dissolved in appropriate solvents the solution kills *Staphylococcus aureus* under test conditions even when diluted 1 part in ten.

Considering the added antiseptic power of boric acid, oil of thyme and the other flavoring constituents, these results are to be expected. However, if we compare the N. F. antiseptic solution with phenol we find this solution has a coefficient of approximately 0.03 instead of 0.14 which it should possess. This fact indicates the loss of germicidal substances.

Bacteriological tests on official antiseptic solution and on certain control samples. Tests are for germicides at 20° C. and 37° C.

ANTISEPTIC SOLUTIONS AT 20° C.

Control.	5 Min.	10 Min.	15 Min.
1:60 Phenol	x	—	—
1:70 Phenol	x	x	x
1:3 Antiseptic Sol. N. F. VI	x (1 min.)	x (3 min.)	x (5 min.) x (10 min.)

	1 Min.	2 Min.	3 Min.	4 Min.	5 Min.
1:2 Antiseptic Sol. N. F. VI	x	x	x	x	x
1:8 Antiseptic Sol. Special I	x	x	—	—	—
1:8 Antiseptic Sol. Special II	x	—	—	—	—

x = growth

Special I is made using N. F. VI Formula except *70* parts *alcohol* and *30* parts *water* and *no* talcum.

Special II is made using N. F. VI Formula except 30 parts alcohol, 25 parts of propylene glycol and water *q. s.* 100 parts. No talcum. The phenol equivalent of the thymol and chlorthymol is still greater than 1:60 phenol. It is equal to 1.75% phenol instead of 1.66% phenol.

ANTISEPTIC SOLUTIONS AT 37° C.

Control.	5 Min.	10 Min.	15 Min.
1:80 Phenol	x	—	—
1:90 Phenol	x	x	x

	1 Min.	2 Min.	3 Min	5 Min.
Antiseptic Solution A 4.5:10	x	x	—	—
Antiseptic Solution B 1:10	x	—	—	—
Antiseptic Solution C 1:10	x	—	—	—
Antiseptic Sol. N. F. VI 1:3	x	x	x	x
Antiseptic Sol. N. F. VI Undiluted	x	x	—	—

x = growth

Antiseptic solution "A" was prepared using all the ingredients present in 100 cc. of the official solution except that no talcum was used and 450 cc. of a 70 per cent water 30 per cent alcohol v/v was used for the solvent. This solution was further diluted by using 4.5 cc. of the above solution in sufficient water to make 10 cc. Actually there is present a 1:10 dilution of the active ingredients which should be present in the official solution.

Antiseptic solution "B" was made using the N. F. VI formula and replacing 25% of water with 25% of propylene glycol. Nothing else was omitted except that no talcum was used. One part of the above solution was diluted with water to make 10 parts for the test.

Antiseptic solution "C" was made from N. F. VI quantities except that the alcohol was increased to 70 per cent and a 1:10 dilution was tested. No talcum was used as a clarifier in the manufacture of antiseptic solution A, B or C, in order to avoid loss by absorption.

Solution B and C has the phenol equivalent in thymol and chlorthymol of 1.4 per cent phenol and a 1:80 solution of phenol is 1.25 per cent; therefore, considering the other antiseptics present, killing should be expected in these two dilutions.

Tests indicate that almost forty per cent of alcohol is required to completely dissolve all the constituents. Also, each ingredient individually is completely soluble in the official solvent. Two of the ingredients may be dissolved in the solvent in several instances, but thymol, chlorthymol, eucalyptol, oil of thyme and menthol are closely related chemically and each is only sparingly soluble; therefore, after thymol and chlorthymol have been dissolved in the liquid, the addition of menthol promptly forms a liquid and refuses to dissolve. Apparently a eutectic is formed. The addition of eucalyptol or oil of thyme also forms an insoluble oily liquid.

There are three possible solutions to this problem: (1) Increase alcohol to about forty per cent, (2) use of the newer non-toxic propylene glycol and (3) finally decrease the flavoring constituents such as eucalyptol and menthol very much and decreasing the thymol and chlorthymol just enough to form a clear solution. Numerous other solvents were tried without any appreciable success. Glycerin is of no practical value in effecting solution.

CONCLUSION.

The formula for antiseptic solution of National Formulary VI needs revision. Materials are wasted and consequently the solution is not as effective as it should be for the quantity of materials used. Either the quantities of antiseptics or the character of the solvent must be changed to avoid this needless waste.

By replacing 25 per cent of the water in N. F. VI antiseptic solution with propylene glycol, a solution is made that mixes well with water, requires no clarifying agent, and may be diluted with two parts of water to form a highly effective germicide. Propylene glycol seems to cause the formation of a more pleasant odor and taste in the product. The problem can also be solved very easily by increasing the alcohol to 70 parts by volume which results in a preparation that mixes clear with all proportions of water and is an effective germicide when mixed with two parts of water. Of course any mouthwash or gargle should be effective long after the recommended dilution has been exceeded in order to take care of the dilution which takes place during use.

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