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IODINE SOLUTION COMPRISING AN OXIDATION-REDUCTION SYSTEM

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6 Claims. (Cl. 167—70)

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This invention relates to germicides and the method of preparing them and more particularly to the improvement of iodine germicides.

The principal object of the invention is to increase the germicidal properties of iodine solutions while reducing their causticity to tissue for any given degree of germicidal strength.

Another object of the invention is to increase the germicidal properties of iodine solutions in the respects mentioned in such a manner that the improved solutions may be kept for long periods of time without deteriorating in any material respect.

Another object of the invention is to accomplish the foregoing objectives in a simple and economical manner.

Still other objects and advantages of the invention will appear from the following detailed description thereof.

In United States Patents Nos. 2,209,454 and 2,271,638, issued to Howard L. Guest, it was disclosed that certain inorganic metallic salts that individually exhibit little or no germicidal activity against certain common micro-organisms can be combined in such a manner that the combination possesses pronounced germicidal properties. The combination of salts disclosed in the first of these patents was a mixture of ferrous sulfate and ferric sulfate. The combination of salts disclosed in the second of these patents was a mixture of ferrous chloride and ferric chloride. While the germicidal properties of these combinations are substantially greater than those of any one of the constituents alone, they are not such that the combinations would be classed as highly germicidal, being roughly equivalent to phenol.

In our United States Letters Patent 2,399,829 of May 7, 1946, we disclosed the certain metallic salts that manifest substantial germicidal properties, such as stannic chloride, are substantially more germicidally active when combined with a soluble inorganic salt of the same or another metal in a relatively lower state of oxidation, even though the added salt possesses little or no germicidal properties when tested alone.

Our conclusions from the many experiments performed in making the inventions described above were that the germicidal properties of any soluble, inorganic, metallic salt are very substantially increased by the addition of another soluble inorganic salt of the same or a different metal if the metal of the added salt is either in a higher or a lower state of oxidation than the metal of the salt to which it is added. We have termed such a combination of salts an "oxidation-reduction system," and this term will be employed in the same sense hereinafter. Experiments involving a large number of combinations of salts comprising many different metals and many different negative radicals have indicated that the

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phenomenon described is a general one, for in no instance was an exception found to the rule that two salts mixed to produce an oxidation-reduction system exhibit a germicidal activity markedly greater than the same salts when tested individually.

The present invention involves the discovery that the germicidal efficiency of conventional iodine solutions can be greatly improved and their toxicity to tissue simultaneously greatly reduced by the addition of a combination of two soluble metallic salts selected to produce between themselves an oxidation-reduction system.

For a more complete understanding of the present invention, reference is made to the following examples of experiments that have been performed to establish the operative character and value of the invention, the specific examples having been selected for illustrative purposes only. In carrying out these experiments, a conventional, standard iodine solution was prepared by dissolving 5 grams of iodine and 10 grams of potassium iodide in sufficient distilled water to make 1000 cc. of solution, this being considered a 1:200 dilution (i. e., 1 gram of iodine to 200 cc. of water). Standard solutions containing selected oxidation-reduction systems were also prepared by dissolving appropriate proportions of the selected salts in distilled water in the amount of 50 grams of the combination of salts in sufficient distilled water to make 1000 cc. of solution, this being considered a 1:20 dilution. Our improved type of iodine solution was then prepared simply by adding a predetermined quantity of the solution containing the oxidation-reduction system to a predetermined quantity of the iodine solution and diluting the resulting mixture as required by the tests performed.

In the examples given hereinafter, comparisons are made of the germicidal effects of a number of solutions on *Staphylococcus aureus* and *Eberthella typhosa* and of the toxicity of the different solutions to tissue. The germicidal and tissue toxicity tests were all carried out in a shaking water bath at a temperature of 37° C., the exposure period being 10 minutes. Twenty-four hour germ cultures were employed, the cultures being standardized in a photoelectric colorimeter. Turbidity standards of barium sulfate were prepared according to the McFarland nephelometric method, and the germ cultures were diluted with broth until they gave the same reading as the No. 7 standard. The tissue toxicity tests were made on embryonic chick heart tissue fragments by the tissue culture technic (Salle, McOmie, Schehmeister, and Foord, J. Bact., 1939, vol. 37, p. 639).

A useful toxicity index for germicides may be defined as the ratio of the highest dilution of germicide that will kill tissue to the highest dilu-

tion that will kill a given test organism under the same conditions. Theoretically, an index less than 1 indicates that the germicide is more toxic to bacteria than to tissue; an index greater than 1 indicates that the germicide is more toxic to tissue than to bacteria. Thus, the smaller the toxicity index, the more nearly perfect is the germicide. Where toxicity indices are mentioned in the following examples, reference is made to the above ratio.

EXAMPLE 1

An oxidation-reduction system comprising 1 mole of manganous sulfate to 1 mole of ferric sulfate was prepared in a 1:20 standard solution as described above. When tested for toxicity to tissue, it was found to kill the tissue fragments in a dilution of 1:2000. The standard iodine solution described above was then subjected to the same test and was found to kill the tissue fragments in a dilution of 1:4000. In order to evaluate the killing dilution of iodine in combination with the oxidation-reduction system, it was necessary to use a more dilute solution of the metal salts. Accordingly, with the oxidation-reduction system dilution maintained at 1:3000 as the iodine concentration was varied, the combination was subjected to the same test and was found to kill the tissue fragments with an iodine concentration of 1:3750.

The killing dilutions of the various solutions for *Staphylococcus aureus* and *Eberthella typhosa* were next determined by the tests described above. The killing dilutions for the

From Table I it is graphically apparent that the combination of the oxidation-reduction system with iodine has a bacteria killing power several times greater than the additive effects of the ingredients; and what is even more unexpected, though the toxicity indices of the oxidation-reduction system are higher than that of iodine alone, the toxicity indices of the combination are considerably lower than those of either of the components alone and indicate that the germicidal efficiency of the combination is approximately four times as great as that of iodine alone.

Because of its very low toxicity, its freedom from bacteriostasis and its cumulative action, the combination of this oxidation-reduction system with iodine promises to be of great value for clinical application as well as general use. On long standing only a slight precipitate forms from the combination with substantially no reduction in its germicidal effectiveness, so that the germicide may be kept for long periods of time without material deterioration.

EXAMPLE 2

A standard solution of an oxidation-reduction system comprising manganous chloride and ferric chloride was prepared by dissolving two moles of ferric chloride to one mole of manganous chloride in distilled water in the amount of 50 grams of the combination of salts in 1000 cc. of the solution (a 1:20 dilution). On repeating the tests of Example 1, the results shown in Table II were obtained.

Table II

Solution	Killing Dilution of I			Toxicity Index	
	Tissue (A)	<i>Staph. aureus</i> (B)	<i>E. typhosa</i> (C)	<i>Staph. aureus</i> (A/B)	<i>E. typhosa</i> (A/C)
Iodine sol. plus O-R (O-R dilution, 1:3000)	1:5,000....	1:120,000...	1:50,000....	0.042	0.1

oxidation-reduction system were 1:75 and 1:1000 respectively. The killing dilutions of iodine were 1:20,000 and 1:17,500 respectively. Since a 1:75 dilution of the oxidation-reduction system killed *Staph. aureus*, it was necessary to combine a more dilute solution with iodine to make it possible to find the killing dilution of the combination. With the oxidation-reduction system dilution maintained at 1:100 the combination killed *Staph. aureus* in a dilution of 1:450,000 of iodine; with the oxidation-reduction system dilution maintained at 1:3000, the combination killed *Staph. aureus* in a dilution of 1:80,000 of iodine and *E. typhosa* in a dilution of 1:60,000 of iodine.

The results of the above tests, together with toxicity indices calculated from those results in the manner described above, are shown in Table I.

Table I

Solution	Killing Dilution			Toxicity Index	
	Tissue (A)	<i>Staph. aureus</i> (B)	<i>E. typhosa</i> (C)	<i>Staph. aureus</i> (A/B)	<i>E. typhosa</i> (A/C)
O-R solution alone.....	1:2,000.....	1:75.....	1:1,000.....	26.60	2.00
Iodine solution alone.....	1:4,000.....	1:20,000.....	1:17,500.....	0.20	0.23
Iodine sol. plus O-R (O-R dilution, 1:3000)	1:3,750.....	1:80,000.....	1:60,000.....	0.05	0.06

Comparing the results shown in Table II with those in Table I, it can be seen that the employment of an oxidation-reduction system composed of manganous chloride and ferric chloride produces an iodine solution somewhat more toxic than iodine alone at the same concentration but so much more toxic to bacteria that its toxicity indices are much lower than those of iodine alone. This oxidation-reduction system produces an iodine germicide slightly better than the combination tested in Example 1, as far as its toxicity characteristics are concerned, because of the greater importance of *Staph. aureus* to which it is more toxic. It is also superior because it is totally free from precipitation and may be kept indefinitely without deterioration. For these reasons, this oxidation-reduction system is preferred to the one tested in Example 1.

In the foregoing examples, the metal in the higher state of oxidation was a different metal than the one in the lower state of oxidation. However, this is not a necessary condition for similar improvements in the efficiency of iodine solutions are obtained when the metallic ions of the oxidation-reduction system are, e. g., ferrous and ferric ions or manganous and manganic ions. While still other metals than manganese and iron may be employed with material improvements in iodine solutions to which they are added, solubility problems make them less desirable.

The phenomenon responsible for the effectiveness of the present invention is a function primarily of the metallic ions present in the oxidation-reduction system. The negative ions apparently play little, if any, part in the reaction and are of little importance except as they effect the solubilities of the metals.

While the oxidation-reduction systems illustrated in the foregoing examples comprised equal molar proportions of the two component salts in Example 1 and two moles of ferric chloride to one mole of manganous chloride in Example 2, these proportions are not critical, though the effectiveness of any oxidation-reduction appears to reach a maximum when the two component salts are mixed in definite proportions that differ for different salt combinations.

The present application is a continuation in part of our copending application Serial No. 501,298, filed September 4, 1943, for "Germicides and Method of Making Same," now abandoned, and is closely related to another of our copending applications, Serial No. 618,060, filed September 22, 1945, for "Phenolic Type Germicides and Method of Making Same," now abandoned.

While the present invention has been illustrated herein by certain specific examples, it will be understood that the invention is not limited to the details of those examples except as may be required by the terms of the appended claims.

We claim:

1. A germicidal solution comprising iodine and a plurality of metallic salts constituting an "oxidation-reduction system," the metallic ion con-

stituents of said salts being selected from the class consisting of iron and manganese and the negative ion constituents of said salts being selected from the class consisting of chlorides and sulfates.

2. An aqueous germicidal solution comprising iodine and the chlorides of divalent manganese and trivalent iron in the ratio of two moles of the iron to one mole of the manganese.

3. A germicidal solution comprising iodine and the sulfates of divalent manganese and trivalent iron.

4. An aqueous germicidal solution comprising iodine and the sulfates of divalent manganese and trivalent iron.

5. An aqueous germicidal solution comprising iodine and approximately equal molal quantities of the sulfates of divalent manganese and trivalent iron.

6. The process of increasing the germicidal properties of iodine that comprises adding to iodine in solution a plurality of metallic salts constituting an "oxidation-reduction system," the metallic ion constituents of said salts being selected from the class consisting of iron and manganese and the negative ion constituents of said salts being selected from the class consisting of chlorides and sulfates.

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REFERENCES CITED

The following references are of record in the file of this patent:

UNITED STATES PATENTS

Number	Name	Date
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2,209,454	Guest	July 30, 1940
2,271,638	Guest	Feb. 3, 1942
2,354,334	Salle et al.	July 25, 1944
2,399,829	Salle et al.	May 7, 1946

OTHER REFERENCES

Proceedings Soc. Exp. Biol. and Med., for January 1944, vol. 55, pages 26, 27 and 28.