

was added until a faint white precipitate was formed. The solution was then clarified and warmed, and mixed with a warm solution of 5.5 Gm. of catechol in 28 cc. of saturated sodium chloride solution. Then saturated sodium carbonate was added to the yellow solution until no further precipitate was obtained. The yellow precipitate was collected on a Buchner funnel, washed with water, alcohol and ether. The yellow solid was insoluble in aqueous sodium hydroxide but was soluble in hydrochloric acid.

The biological tests on these compounds were carried out in the Biological Laboratories of E. R. Squibb and Sons, New Brunswick, N. J.

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RESEARCH DEPT. OF THE CHEMICAL & PHARMACEUTICAL LABORATORIES,
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A STUDY OF SOME INCOMPATIBILITIES OF QUININE SULPHATE.

BY ALFRED BARTHEN, HERMAN EISENBERG AND FRANK A. LEE.

This paper is the result of a study of the incompatibilities that take place when quinine sulphate in aqueous solution is treated with any one of the following substances: Hypophosphorous acid, citric acid, acetic acid and an excess of the corresponding potassium salt is added to the mixture; also the incompatibility that results when quinine sulphate solution is treated with a solution of sodium salicylate. It has been stated that the corresponding quinine salt of the acid radical used is the substance precipitated, but in view of the fact that the acid mixture itself does not precipitate, and only after the corresponding potassium salt of the acid radical in question has been added that the actual precipitation is noticed, there is the possibility of the formation of a complex compound in each case, rather than the normal quinine salt. It was to investigate this possibility that the work was started.

EXPERIMENTAL PART.

QUININE ACETATE (1, 2).

Ten grams of quinine sulphate was added to 20 cc. of distilled water and 11 cc. of glacial acetic acid, producing a clear solution. To this solution was added 15.5 cc. of a solution of potassium acetate containing 12 Gm. of the salt. A voluminous precipitate formed immediately. The mixture was allowed to stand several hours to insure complete precipitation. The resulting precipitate was placed on a filter and washed until free from sulphates. It was dried on a porous plate and kept in a desiccator over sulphuric acid.

Qualitative tests showed that the precipitate contained the quinine and acetate radicals. When the compound was ignited, it first evolved a peculiar fruity odor. It then blackened simultaneously with the liberation of a gas. On the application of continued and higher heat, it was found that no residue remained, indicating the compound to be entirely organic.

Quantitative work showed the product to contain the percentages of quinine and acetate calculated for the salt quinine acetate.

This shows that textbooks need not be hesitant about stating the composition of the precipitate as quinine acetate.

QUININE CITRATE (3, 4, 7).

Ten and one-half grams of quinine sulphate was added to 30 cc. of distilled water containing 15.75 Gm. of citric acid: this mixture resulted in a clear solution. To this solution was added 25 cc. of a solution of potassium citrate containing 16 Gm. of the salt. A voluminous, heavy precipitate formed immediately. This was allowed to set and then filtered and washed free from sulphates. It was then dried on a porous plate and preserved in a desiccator as given under quinine acetate.

Ten and one-half grams of quinine sulphate was added to 30 cc. of distilled water containing 15.75 Gm. of citric acid: this mixture resulted in a clear solution. To this solution was added 25 cc. of a solution of potassium citrate containing 16 Gm. of the salt. A voluminous, heavy precipitate formed immediately. This was allowed to set and then filtered and washed free from sulphates. It was then dried on a porous plate and preserved in a desiccator as given under quinine acetate.

The precipitate responded positively to qualitative tests for the quinine and citrate groups. Upon ignition, the compound left no residue, demonstrating its freedom from potassium additive compounds.

Quantitative analysis showed that the substance was quinine citrate.

QUININE HYPOPHOSPHITE (4).

One hundred and fifty cc. of distilled water was added to 56.5 Gm. of quinine sulphate and 20 cc. of 50 per cent hypophosphorous acid, producing a clear solution. To this solution was added 100 cc. of a concentrated solution of potassium hypophosphite, made by dissolving 120 Gm. of potassium hypophosphite in 72 cc. of distilled water. A voluminous precipitate resulted to which was added 100 cc. of distilled water. The mixture was filtered and the residue thoroughly washed with distilled water. The precipitate was dried on a porous plate and stored in a desiccator.

The resulting compound when heated evolved a peculiar odor, and upon ignition, blackened with a liberation of the obnoxious, spontaneously combustible gas, phosphine. On further heating, the compound burned entirely without leaving a residue, demonstrating that a potassium additive compound was not formed. The substance responded to qualitative tests for quinine and for hypophosphite.

Quantitative determinations for phosphorus and quinine identified the compound as quinine hypophosphite.

QUININE SALICYLATE (5, 6).

Fourteen grams of quinine sulphate was treated with 100 cc. of distilled water; the mixture was heated to boiling and precipitated with 5.45 Gm. of sodium salicylate dissolved in 42 cc. of distilled water. The resulting material was cooled, filtered and the residue was washed free of sulphates. The product was dried and put into a desiccator.

The compound left no residue on ignition, showing that an additive compound could not have been formed. It responded to qualitative tests for the quinine and the salicylate radicals.

Quantitative work showed it to be quinine salicylate.

DISCUSSION OF RESULTS.

Considering the conditions under which the precipitates described in the experimental part were formed, it might seem possible that a complex compound in each case could be produced, especially in the first three cases. The precipitate was produced in each of these after the addition of the corresponding potassium salt. It was found, however, in all of these cases that the precipitation was probably brought about by common ion effect rather than by the production of an additive or a complex compound of some sort.

It is known that under different conditions of precipitation, such as might be found in different prescriptions, the physical character of the precipitate varies. Chemically, however, it was found to remain the same in the cases and under the conditions tried.

The results show that textbooks need not hesitate to state the composition of the precipitates that are formed as given in the foregoing report.

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Professor Olsen says, in an article on how changes occur in the practice of retail pharmacy and to make it clear that over-extensions and unjustified developments inevitably correct themselves: "Good judgment and honest common sense ultimately prevail. That's the cheering thing about the future we now face."
