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Dr. Francis C. Frary
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Post Office Box 772
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Dear Dr. Frary:

Your good letter of the 21st indicates that you are already making good your offer to "be of further assistance" and both are appreciated.

I fear that I am going to make a nuisance of myself because of my ignorance of the physical chemistry of aluminum compounds and because of my conviction that alterations of solubility of quartz in vitro do not parallel the evidences of protective action obtained empirically by animal injections. In fact our own observations have disclosed many conditions that are at variance with the solubility hypothesis of the action of quartz in the body.

We, for example, have injected a great number of silicates into animals which yield more soluble silica in the test tube than quartz and yet these silicates have provoked no fibrosis or any other serious reaction. Our comparative tests of solubility were made upon as pure minerals as it was possible for an experienced petrographer to select and, what was equally important, upon elutriated particles of a standard size range of 1 to 3 microns.

Like Dr. Irwin, we have repeatedly made tests of the depression of solubility of quartz by adding other minerals but the severity of tissue reaction never corresponds with the percentage reduction in soluble silica. A case in point is the acetone washed metallic aluminum powder (A-11) furnished us by Dr. Irwin at the outset of our experiments. It was mixed with different samples of Ontario quartz under the same conditions used in Toronto for determinations of soluble silica. Our results were very similar to Dr. Irwin's. With one sample of quartz we obtained 92.6 parts per million soluble silica and he found 84. With another ours was 102.6 and his 105. Addition of aluminum in the recommended proportions reduced these solubilities by 99.6 and 99.2 per cent respectively.

We have kept this tube of powder in the laboratory for over three years and last week tested its effect upon the same samples of quartz. Again the respective reductions in solubilities were 97.1 and 98.8 per cent. Our own quartz, with which all animal experiments are made, is a much purer material yielding 99.7 per cent SiO_2 on chemical analysis and no lines except those for normal quartz on x-ray diffraction. In water under comparable conditions it gave only 8.9 parts per million soluble silica with a depression of solubility of 95.5 per cent on the addition of the aluminum in same quantities.

In spite of the very obvious decrease in the per cent of soluble silica resulting from the addition of the aluminum powder in the test tube the latter substance in four separate animal experiments had no effect upon the usual reactions produced by our quartz dust. Two of these were made with the unheated powder after we had learned of the possibility that heat might destroy its protective action. I could only infer that in aging the powder had been oxidized to such an extent that it no longer inhibited quartz, or that possibly there were peculiarities in our water, although it was distilled in glass, which were different from those of the Toronto supply.

On the other hand we have obtained evidence of highly satisfactory protective action with the two forms of aluminum hydroxide about which I first wrote you and their effect upon the solubility of quartz in the test tube are essentially the same. With it the percentages of reduction in solubility of the two above mentioned Ontario quartz were 97.6 and 99.5 respectively. In a long series of experiments with the hydroxide which were started independently of the Ontario work some six months before we had heard of their work, we have repeatedly found that animals were as completely protected against silicosis as those treated with the metal by Denny, Robson and Irwin. Most of our tests were made by injecting both the quartz and the hydroxide in order to establish principles governing the behavior of the two chemicals in the living body. We were finally confronted with the practical test of getting the inhibitor substance into the lungs, where human silicosis develops, and concluded, as did the Ontario group, that inhalation was the only practical means of accomplishing this purpose. Then came the problem of finding a form of the hydroxide that was stable and would make an inhalable dust. This prompted the questions of my first letter to you.

We need help in determining the exact nature of the compounds with which we have already worked and for that reason I shall take the liberty of describing our procedure in the preparation of these compounds and, under separate cover, am sending you a sample of the material that we have called "dry, powdered aluminum hydroxide precipitate".

The colloidal solution was prepared as follows:

To 500 c.c. of distilled water add 15 gm $AlCl_3 \cdot 6H_2O$.

Boil and add slowly NH_4OH until a distinct odor of ammonia persists and no more precipitate forms.

Filter and wash residue with hot water until no test for chlorides is obtainable.

Take care that the residue does not dry on the filter.

Resuspend residue in 500 c.c. of distilled water.

This milky colloidal solution is non-dialysable and has a pH of 5.8 to 6.4.

To form the precipitated powder, proceed as before but then allow the chloride-free residue on the filter paper to dry in air at room temperature.

Remove to an evaporating dish and place in vacuo at room temperature for 48 hours.

Grind in an agate mortar and suspend in water for injection into animals.

We have supposed that both of these products were trihydrates as the latter one had not been subjected to heat in the process of drying. We know that they are stable because both of them have given good protection in animals a year or more after they were made. If the latter one should prove to be a substance which can be produced cheaply and our inhalation test demonstrates that it forms an inhalable dust it might constitute a substitute for the metal which apparently must be freshly ground to be of benefit.

Before going further, however, we must prove its inhalability, check its effect upon the lungs of silicotic animals and above everything prove whether it influences susceptibility to associated tuberculosis. This will give us plenty of business to carry along parallel with the experimental study of the human subjects.

From this presentation of my problem you may infer that my immediate need is an identification of the material with which we have done so much work. We shall unquestionably want to try the effect of these other products, "C-730 Aluminum Hydrate" and the activated variety mentioned in your letter. But as the only reliable method of testing that I now know of involves a year's observation on animals I am hesitant to undertake it at once.

The Ceramics Society has asked me to talk about protective action at the Baltimore meeting on Wednesday afternoon, April 2. I shall show a few lantern slides to demonstrate what the hydroxide will accomplish and then discuss an experiment in which a sagger mixture, containing 50% free silica, caused no silicosis in animals. Their clays, even after calcination, I believe are good protectors. I hope sooner or later to study a number of them. Should you be planning to attend this meeting, I hope that I may have an opportunity to talk with you. Again may I thank you for your help and advice.

Sincerely yours,

Leroy U. Gardner, M.D.
Director

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