Quality of Radioiodine

The increasing use of lactoperoxidase for the iodination of proteins and cell surfaces makes it important to point out to users and would-be users of this method an interesting and disturbing phenomenon which I have observed. Those new to the technique might become discouraged with the lactoperoxidase system if they discover that their proteins iodinate poorly or not at all. The problem may in fact lie with the ^{125}I, not with the technique.

At least a year ago D. Gospodarowicz of the Salk Institute informed me that the efficiency of soluble lactoperoxidase iodinations carried out in the absence of carrier iodide varied greatly depending on the source of $Na^{125}I$. This variability was not observed if he iodinated his protein in the presence of carrier iodide; incorporations were then uniformly high. Of the radioiodide suppliers which he tried, New England Nuclear (NEN) provided $Na^{125}I$ that gave the greatest carrier-free iodination efficiency (about 90 to 95 percent), while other sources supplied much poorer iodide (as low as 10 percent efficiency of incorporation for ^{125}I). Since my radioiodine source had long been NEN (for other reasons) I had never noticed the problem while working with the solid state lactoperoxidase system.

We routinely iodinate carcinoembryonic antigen (CEA) with solid state lactoperoxidase, using carrier-free $Na^{125}I$, to a specific activity of about 20 to 30 $\mu c/\mu g$. When we iodinate 5 μg of CEA, we obtain an iodination efficiency of roughly 40 percent ^{125}I incorporation. About 3 months ago, we suddenly lost the ability to iodinate CEA with our lactoperoxidase. The enzyme was good, since ^{131}I incorporations were normal. Rabbit immunoglobulin G (IgG) iodinated very poorly with $Na^{125}I$ in the absence of carrier iodide; but when a 100-fold excess of carrier KI was employed (at the same ratio of IgG to total iodide), the efficiency of incorporation returned to almost normal, very reminiscent of the results described by Gospodarowicz. I am told that chloramine-T iodinations are not affected by whatever is inhibiting the lactoperoxidase iodinations—with or without carrier. I have heard several informed accounts, however, that many enzymes and hormones rapidly lose biologic or antigenic activity after iodination with this "bad" ^{125}I.

Conversations with R. J. Thomas of NEN disclosed the fact that NEN (and apparently certain other radioisotope distributors as well) was temporarily unable to obtain $Na^{125}I$ from its usual supplier and had been forced to resort to an alternate ^{125}I producer. Presumably the difference in iodination characteristics when carrier-free ^{125}I as noted above was used resulted from differences in the quality of $Na^{125}I$ obtained by NEN from the two different radioiodine sources. Apparently there exists a production procedure for ^{125}I which results in a low ^{126}I content. It would appear that a secondary effect of this process may be to yield a radioiodide vastly more suitable for lactoperoxidase iodinations. The developers of this method of production are not anxious to publicize their procedure, nor has anyone been able to suggest the nature of the contaminating material responsible for the inhibition of lactoperoxidase iodinations.

"Good" $Na^{125}I$ is once more available from NEN, and, I presume, from other distributors. Our laboratory lost considerable time and money while the problem existed, however, and we cannot be assured this will not happen again. Apparently NEN is now aware of the magnitude of the problem, but they can only warn us if this situation arises again. Since I can understand the unwillingness of their suppliers to disclose details of the superior method of ^{125}I production, it seems that the only route open to us is to determine the nature of the impurity (or impurities) in the "bad" $Na^{125}I$ and to try to remove them ourselves, or to request the producers of this material to remove them prior to distribution.

The advantages of using lactoperoxidase for the iodination of many proteins have been demonstrated a number of times (*1*). It is unfortunate, however, that this useful technique should be limited by the quality of radioisotope available.

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References

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During the period from 26 September to 26 November 1973, New England Nuclear Corporation was forced because of a labor dispute to obtain ^{125}I from a secondary source. This material was subjected to our normal quality control, which includes chromatography to determine the oxidation state and several routine Chloramine-T iodinations of proteins. The results of these tests did not lead us to the conclusion the ^{125}I was "bad." The only difference that we could determine in the quality of the ^{125}I from the alternate source was the higher ^{126}I content.

Our experience has shown that some lots of ^{125}I behave normally in our hands, but lead to poor iodination in the hands of others who could be using the ^{125}I in more sensitive iodinations.

NEN is actively seeking criteria to minimize experiences such as reported by David. The line between "good" and "bad" iodine is not clearly defined, because of the many uses to which the product is being subjected. We appreciate David's comments and welcome comments from the scientific community regarding further criteria that can be used to determine the quality of ^{125}I for all iodination techniques.

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