LETTERS TO THE EDITOR

Re: Stability of Stannous Ion in Stannous Pyrophosphate Kits

Recently a letter in the *Journal* from Huberty and Hattner (*1*), dealing with modifications in the method of in vivo labeling of red blood cells with Tc-99m, pointed out that this method of RBC labeling with cold Sn-PPi is extremely sensitive to kit quality. Their letter states that for the purpose of in vivo RBC labeling, "Sn-PPi kits more than 90 days old should not be used nor should preparations reconstituted more than 90 minutes earlier." They provide no substantiating data for these statements, but the inference is strong that Sn(II), the labile reduction component, is sufficiently unstable with time to prejudice the RBC labeling capabilities of Sn-PPi kits.

In this light, we examined several different lots of Sn-PPi with varying expiration dates to determine the stannous ion content and to determine the extent of stannous ion degradation with time after reconstitution of Sn-PPi kits with normal saline. Our method involved indirect potentiometric titration (*2–3*), using whole-vial Sn(II) measurements made by dissolving the lyophilized powder in 1 ml of 0.1 *M* $FeCl_3 .6H_2O$ and 2.4 *M* HCl. This method converts Sn(II) to an equivalent amount of Fe(II), which is more stable against air oxidation during titration. Each sample was quantitatively transferred to a 15-ml beaker with 3.0 ml distilled water. Hydrochloric acid (12 *M*), in 3.6 ml, is added just before titration with standard 0.01 *N* potassium dichromate solution. One milliliter of 0.01 *N* $K_2Cr_2O_7$ is equivalent to 0.59345 mg Sn(II).

For the time-dependent study, 5 ml of normal saline was used to reconstitute each kit. At predetermined time intervals, 0.2-ml samples were obtained with a microliter pipette and added to 2 ml of 6 *M* HCl containing 0.1 ml of the $FeCl_3$ solution. The sample was titrated with 0.001 *N* $K_2Cr_2O_7$. During all steps, care was taken not to introduce air into the vial. After 18 hr, 3 ml of air was introduced into the vial, and 0.2-ml samples were taken at selected time intervals and assayed for Sn(II) content to determine the effect of air on Sn(II) stability.

The results of the whole-vial assay appear in Table 1, and show that Sn(II) content varied from 79–91% of the theoretical amount stated on the vial label. In our findings, there was no correlation between the amount of Sn(II) content and the age of the kit. In fact, the newest lot of Sn-PPi had the lowest percentage of Sn(II). Tables 2 and 3 indicate the Sn(II) stability with time for solutions tested under both nitrogen and room air. For this portion of the study, the newest lot of Sn-PPi was tested. It is evident from Table 2 that less than 10% degradation of Sn(II) occurs up to 3 hr after reconstitution with saline under nitrogen, and 86% of the Sn(II) was still present by 18 hr. When 3 ml of room air was injected into the 18-hr-old vial, the amount of Sn(II) remaining at the end of an additional 8 hr was within 85% of the Sn(II) content before the addition of room air.

From our study, we conclude that no significant differences exist among Sn(II) content in Sn-PPi kits more than 90 days old and, although Sn(II) content did vary among different lots, the most likely explanation involves variations in vial filling by the manu-

TABLE 1. STANNOUS ION CONTENT IN Sn-PPi KITS

PPi lot	Exp. date	Assayed Mg. Sn (II)	% Theoretical Sn (II)*
0941014A	Oct. 81	1.731	81.3
0941035B	Apr. 82	1.929	90.6
0942013B	Oct. 82	1.892	88.9
0944038A	Mar. 83	1.682	79.0

* Based upon theoretical Sn (II) of 2.128 mg/vial of Technescan PYP.

TABLE 2. LOSS OF Sn (II) IN Sn-PPi SOLUTION (LOT #0944038A) IN VIAL (UNDER NITROGEN)

Time (hr)	μg Sn (II) assayed	% Theoretical yield*
0	64.30	95.6
0.5	61.82	91.9
1.0	60.59	90.0
2.0	61.82	91.9
3.0	61.82	91.9
18.0	58.11	86.4

* Based upon 1,682 μg Sn (II)/5 ml; 0.2 ml samples = 67.28 μg Sn (II).

TABLE 3. LOSS OF Sn (II) IN Sn-PPi SOLUTION (LOT #0944038A) BEGINNING 18 hr AFTER RECONSTITUTION WHEN 3.0 ml ROOM AIR WAS ADDED

Time (hr)	μg Sn (II) assayed	% Theoretical yield*
0	58.11	100
0.5	58.11	100
2.0	54.4	93.6
4.0	51.9	89.4
8.0	49.5	85.1
72.0	14.8	25.5

* Based upon initial (zero time) sample. Room air added at zero time.

facturer during preparation. We also failed to note any significant effect of reconstitution time upon Sn(II) content.

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REFERENCES

1. HUBERTY JP, HATTNER RS: Re: A modified method for the in vivo labeling of red blood cells with Tc-99m. (lett) *J Nucl Med* 23:945-946, 1982
2. COLLINS RW, NEBERGALL WH: Indirect procedure for the determination of tin (II) by potentiometric titration. *Anal Chem* 34:1511-1513, 1962
3. KOWALSKY RJ, DALTON DR: Technical problems associated with the production of technetium Tc-99m tin (II) pyrophosphate kits. *Am J Hosp Pharm* 38:1722-1726, 1981

Reply

Kowalsky and Chilton have shown that the desired oxidation state of tin is maintained in Sn-PPi kits at various times after reconstitution and kits more than 90 days old. However, they have not shown that the Sn(II) is a chemically viable species. In fact their results would be similar whether stannous chloride, stannous oxychloride colloid, or stannous pyrophosphate were evaluated. Our *Journal* letter of October, 1982 (*1*), expressed concern regarding the status of pyrophosphate as an effective masking agent (*2*) in kits more than 90 days old. We did not base our comments on the oxidation state of Sn(II), but on its chemical state in Sn-PPi kits and on the incidence of hydrolytic by-products of Sn(II) secondary to ineffective masking.

Historically it has long been known (A. Reynoso-1852; H. Giren-1903) that pyrophosphate suffers from entropic doom and that this hydrolytic degradation is governed by pseudo-first-order kinetics (*2-4*). Lyophilization, unfortunately, does not remove all water. Furthermore, the effect of pH has been studied (*5,6*) as well as addition of neutral salts (*5-7*) and the influence of strongly coordinated cations (*7*).

For these reasons, and having investigated the properties of Sn-PPi kits (*8*), we limit Sn-PPi use to 30 days after manufacturing and 30 min after reconstitution with pertechnetate. This product is further limited to in vivo RBC labeling that requires a Sn(II) content of 15 μg to 20 μg per kg body weight. In vitro RBC labeling is performed using Sn-MDP or Sn-citrate. Myocardial infarction studies are performed very successfully using imidodiphosphonate (IDP).

Perhaps a more effective analytical technique to evaluate this compound would involve the use of HPLC and ion chromatography HPLC.

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REFERENCES

1. HUBERTY JP, HATTNER RS: Re: A modified method for the in vivo labeling of red blood cells with Tc-99m. *J Nucl Med* 23:945-946, 1982
2. PERRIN DD: The selection of masking agents for use in analytical chemistry, In *Critical Reviews in Analytical Chemistry*. CRC Press, 1975, pp 85-117
3. ABBOTT GA: Ionization relations of ortho and pyrophosphoric acids and their Na salts. *J Am Chem Soc* 31:729-763, 1909
4. KIEHL SJ, CLAUSSEN E: Temperature coefficients in the acid hydration of Na pyrophosphate. *J Am Chem Soc* 57:2284-2289, 1935
5. CAMPBELL DO, KILPATRICK ML: A kinetic study of the hydrolysis of pyrophosphates. *J Am Chem Soc* 76:893-901, 1954
6. VAN WAZER JR, GRIFFITH ED, MCCULLOUGH JF: Structure and properties of the condensed phosphates VII. Hydrolytic degradation of pyro- and tripolyphosphate. *J Am Chem Soc* 77:287-291, 1955
7. KAILEN A: Rate of hydrolysis of phosphoric acid. *J Am Chem Soc* 160a:301-303, 1932
8. HUBERTY JP, HATTNER RS, POWELL MR: A ^{99m}Tc-pyrophosphate kit: A convenient, economical and high-quality skeletal-imaging agent. *J Nucl Med* 15:124-126, 1974

Perchlorate Blocking for Radioimmunodetection

Tumor detection using radiolabeled antibodies (RAID) is an important new technique (*1*) that is being applied in many centers. To date iodine isotopes have been the labels of choice because of their useful physical and biological characteristics and the simplicity of attaching them to proteins. However, the iodine is rapidly split from the antibody in the tissues, and unless preventative steps are taken it accumulates in the thyroid, stomach, salivary glands, and other organs, giving confusing results. Furthermore, damaging radiation doses to these organs may occur.

The usual technique for blocking radioiodine uptake is to give a large oral dose of stable iodide (KI) of ~ 500 times the normal daily intake of iodine (0.5 mg), but in practice, perhaps for reasons of poor intestinal absorption, this is insufficient to block all radioiodine uptake (*2*). Furthermore, pertechnetate (TcO_4^-), which is used as a subtracting tracer in RAID, has a much higher affinity (times 50 to 100) than iodine for the transport mechanisms (*3*) so blocking with iodide is even more difficult. This adds to the difficulties of both scan interpretation and radiation dose.

To overcome these problems we give potassium perchlorate ($KClO_4$) in addition to KI. $KClO_4$ has an affinity similar to TcO_4^- for the iodide transport mechanisms, and can block stomach and salivary uptake of both radionuclides.

We use the following regimen: 30 min before the antibody injection, 420 mg of KI is given and thereafter 60 mg every 4 hr, with 120 mg at night, for 2 days; 2 hr before each study, 1 g of $KClO_4$ is given, which can split into four doses daily. After the last study the KI is reduced to 60 mg twice daily for 1 wk and no further $KClO_4$ is administered.

Using this regimen we have found that there is minimal radioiodine uptake in the stomach and salivary glands and little iodine accumulation in the gut. This gives us much greater confidence when interpreting images of the head and neck, stomach, pancreas, left lobe of the liver, and other abdominal organs. The only notes of caution are that the patients may experience nausea (in which case the $KClO_4$ doses should be divided) and allergic manifestations may rarely occur if the doses are extended beyond the period suggested.

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