

The Chemical Identity of Pentavalent Technetium-DMSA and Editorial: Small Coordination Complexes in Tumor Imaging

TO THE EDITOR: In his editorial (1) discussing the prospects for use of small coordination complexes in tumor imaging, Dr. Abrams refers to the conclusions of our study "The chemical identity of pentavalent technetium-99m-DMSA" (2). He points out that our conclusion that pentavalent Tc-99m-DMSA is an isomeric mixture of the $\text{TcO}(\text{dithiolate})_2^-$ class is inconsistent with the gel permeation results of Horiuchi et al. (3). The latter authors concluded that the species was a high molecular weight polymer. In fact, we have already addressed experimentally this apparent anomaly, and our results were discussed in the original manuscript sent to *JNM*. However, following pressure from a referee, this material was removed to reduce the length and chromatographic content of the manuscript. The mention of the inconsistency by Dr. Abrams suggests that perhaps we made an error of judgement in omitting this material. The essence of our results and discussion of this matter is given below.

Horiuchi et al. concluded that $^{99\text{m}}\text{Tc}(\text{V})\text{DMSA}$ is a high molecular weight polymeric species, on the basis of the observation that it was poorly retained by a Sephadex G15 gel permeation column when eluted with saline. We have repeated their experiment, and our results agree with theirs. On the other hand our results with other chromatographic and electrophoretic methods suggest a monomeric structure. This apparent anomaly requires explanation. To this end, we repeated the gel permeation experiment using a macroscopic sample of $^{99}\text{TcO}(\text{DMSA})_2^-$ (the structural identity of which is not in doubt), using u.v. spectrophotometry to monitor the column effluent, and found that as with the $^{99\text{m}}\text{Tc}$ complex, the complex was eluted within the void volume.

Thus, it appears that gel permeation is not a reliable method for distinguishing small, highly charged molecules on the basis of

size or molecular weight. According to the manufacturer's notes (4), the stationary phase in gels of this type contains a number of residual carboxylate groups which take part in interactions on the basis of charge rather than molecular size. Thus, a highly anionic species such as the present technetium complex which has an average charge approaching -5 at neutral pH, would interact unfavourably with the stationary phase, and therefore elute rapidly, even though on size grounds alone it would be expected to be retained. Accordingly, we carried out the chromatography using high ionic strength formate buffer (0.05 M formic acid/ 0.5 M sodium chloride, pH 3), so that the effects of negative charge on both stationary phase and technetium complex are minimised. Under these conditions, the complex is retained and has an elution volume of $>300\text{ ml}$. We conclude that the gel permeation behavior is not at variance with our proposed formulation.

REFERENCES

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