# Effects of increasing polymer hydrophobicity on distribution ratios of $TcO_4^-$ in polyethylene/poly(propylene glycol)-based aqueous biphasic systems

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## Abstract

The partitioning behavior of the pertechnetate anion was studied in aqueous biphasic systems (ABS) formed from $(NH_4)_2SO_4$ and four types of polymers – poly(ethylene glycol) (PEG), poly(propylene glycol) (PPG), Pluronic (a PEG/PPG block copolymer), and polyvinylpyrrolidone (PVP). Phase diagrams are reported for five $(NH_4)_2SO_4$–polymer ABS systems including the polymers PEG-2000, PEG-3400, PEG-12 000, Pluronic-L64 (average molecular mass $\approx 2900$), and PVP-K15 (average $M_r \approx 10\,000$). Distribution ratios for the $TcO_4^-$ anion in each of these ABS were investigated as a function of increasing salt concentration. In addition, the water-insoluble polymer PPG-2000 was studied. Pertechnetate partitions nearly quantitatively to the polymer-rich phase in each ABS, however, distribution ratios of near one were found for the PPG system. The relative ordering of the distribution ratios is PPG≪PVP≪PEG-2000<PEG-3400≈PEG-12 000<Pluronic-L64. For the three PEG-ABS systems, distribution ratios of the sulfate anion decrease in the order PEG-2000>PEG-3400> PEG-12 000, exhibiting the expected increase in phase incompatibility with increasing polymer $M_r$. Investigation of pertechnetate partitioning in two additional ABS based on $K_3PO_4$ and NaOH with Pluronic-L64 revealed trends similar to those reported for PEG-2000; the distribution ratio ($D$) values increase in the order NaOH<$(NH_4)_2SO_4$<$K_3PO_4$. Despite the higher distribution ratios from Pluronic-L64 at lower concentrations than found for PEG, the limited useable range of salt concentrations available may limit the practical utilization of this polymer in ABS separations.

*Keywords:* Distribution ratio; Partitioning; Pertechnetate

## 1. Introduction

The importance of the pertechnetate anion, $TcO_4^-$, in real-world separations cannot be understated. In radiopharmacy the short-lived $^{99m}Tc$ is used in the vast majority of all medical procedures utilizing radioisotopes [1–4]. $^{99}TcO_4^-$, present in the highly alkaline waste storage tanks at such sites as Westing-house Hanford and Savannah River, is a fission product in nuclear fuel burn-up. Its long half-life and environmental mobility present long-term storage problems [5,6].

Because of our promising preliminary results which indicated that pertechnetate would partition nearly quantitatively to the poly(ethylene glycol) (PEG)-rich phase in a variety of salt–polymer aqueous biphasic systems (ABS) in the absence of any added complexants [7–10], we chose to make per-technetate the cornerstone of our partitioning studies. The information gained from these experiments has

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not only helped us to explain $TcO_4^-$ behavior, but has helped us to develop some predictive models which have been successfully applied to the partitioning of other metal ions, and has led directly to the discovery of new salt systems [e.g., $VO_4^{3-}$, $CrO_4^{2-}$, $MoO_4^{2-}$, $WO_4^{2-}$, $HEDPA^{4-}$ (hydroxyethane-1,1-diphosphonate tetra-anion) etc.] capable of forming ABS with PEG [7,11].

The partitioning behavior of $TcO_4^-$ has been investigated as a function of salt used to generate the biphase, salt concentration, PEG molecular mass, pH, and temperature [9–11]. We have been able to demonstrate that partitioning behavior correlates to phase incompatibility as others have observed for neutral solutes [12–15]. We have explained pertechnetate's preference for the PEG-rich phase because of its large, relatively hydrophobic nature and the small value of its estimated Gibbs free energy of hydration ($\Delta G_{hyd}$) [16].

We were also able to correlate the phase forming salt's ability to salt out PEG and thus its influence on technetium distribution ratios ($D_{Tc}$) with the anion's $\Delta G_{hyd}$ [17]. As $\Delta G_{hyd}$ becomes more negative, an anion salts out more PEG. We have also shown that the cations can influence phase composition and $D_{Tc}$ based on their $\Delta G_{hyd}$. Although their effect is smaller than the anions', the cations can be utilized to 'fine-tune' phase characteristics.

Our work initially focused on PEGs because of their low cost, low toxicity, and ready availability. In retrospect, the relative hydrophilicity of the PEGs turned out to be a major factor in the success of our separations. The choice of polymer need not be restricted to PEG, however, and judicious choice of polymer could lead to enhanced separation or stripping.

It may be possible to fine-tune the polymer-rich phase by choosing from a variety of commercially available polymers whose hydrophobicity increases as PEG<Pluronic [block PEG/poly(propylene glycol) (PPG) copolymers]<poly(tetramethylene glycol) [18–22]. This report represents our initial work aimed toward controlling pertechnetate distribution ratios by utilization of polymer hydrophobicity. It includes pertechnetate partitioning data in systems prepared with PEG-2000, PEG-3400, PEG-12 000, Pluronic-L64, polyvinylpyrrolidone (PVP)-K15, and PPG-2000. For these intial studies, ammonium sulfate was chosen as the salting-out agent because of its good solubility range and excellent salting-out ability.

## 2. Experimental

PEG-2000, PEG-3400, PEG-12 000, $(NH_4)_2SO_4$, $K_3PO_4$, and NaOH were purchased from Aldrich and used as received. PPG-2000, Pluronic-L64 (average molecular mass $\approx 2900$) and PVP-K15 (average molecular mass $\approx 10\ 000$) were obtained from Fluka and used as received. All water was purified using commercial deionization systems. $^{99}Tc$ (Amersham) was purchased and used as an aqueous $NaTcO_4$ solution.

Phase diagrams were determined by turbidimetric titration [23]. Systems with compositions in the two-phase region were weighed into tubes. Water was gradually added with vortex-mixing until the turbid mixture just cleared. The final mass of the system was determined and the compositions of the points of phase transition were calculated.

All polymer and salt stock solutions were prepared on a weight percent or molal basis. The compositions referred to in the Discussion are for pre-equilibrium stock solution concentrations. Equal aliquots (750–1000 $\mu$l) of polymer stock solution and salt stock solution were combined. The systems were pre-equilibrated by vortex-mixing for 2 min followed by 2 min of centrifugation. Tracer quantities of $Na^{99}TcO_4(aq)$ (or $H_2^{35}SO_4$) were added and the system centrifuged then vortex-mixed for 2 min. (The contact time was experimentally determined to be sufficient for these systems to reach equilibrium.) The phases were disengaged by 2 min of centrifugation and were carefully separated. Equal aliquots of each phase were then submitted for standard liquid scintillation analysis. All measurements were carried out at least in duplicate.

The radiometric distribution ratio ($D$) is defined as the counts per minute (cpm) in the upper polymer-rich phase divided by the cpm in the lower salt-rich phase. (In the studies involving PVP, the polymer-rich phase was the lower phase.) Radiometrically determined distribution ratios are generally accurate to $\pm 5\%$; however, due to the complexity of these ABS, a conservative accuracy of $\pm 10\%$ is reported.

## 3. Results and discussion

Choice of polymer in an ABS can be a critical factor in the successful execution of a desired separation. This is true not only because of the effect of the polymer on the distribution of the solute between the phases, but also because of the effect the polymer has on the physical characteristics of the ABS. We initially began working with PEG-2000–salt systems because phase separation times, viscosities, etc., were within the range known for traditional oil/water solvent extraction. Thus, while we investigate the effects of different polymers on distribution ratios, we must also make sure that any improvements are not obviated by poor phase characteristics.

The polymers studied in this report, PEG, PPG, PVP, and Pluronic, are depicted in Fig. 1. The PEGs and PVP-K15 were studied using 40% (w/w) stock solutions. PPG-2000 is essentially water insoluble (and thus was utilized neat), but is included for comparison with the ABS systems. The Pluronic polymer used, L64, has a very narrow range of

usefulness. At low polymer and salt concentrations it forms a monophasic system. If the concentration of polymer and salt is too high, the polymer tends to foam out of solution. A workable range for the comparative studies carried out here was found at 15% Pluronic stock solution and $(NH_4)_2SO_4$ stock solution concentrations of 1.6 to 1.9 m.

The viscosities of the polymer-rich phases increased with increasing salt concentration. PEG-2000 ABS gave the least viscous polymer-rich phase, followed by PEG-3400$\approx$PVP-K15<PEG-12 000< Pluronic-L64<PPG-2000. Pluronic-L64 and PVP-K15 actually took the longest time to disengage phases by gravity settling. The phases in the systems containing PEG-12 000 and PPG-2000 separated the fastest, followed in order by PEG-3400<PEG-2000<PVP-K15$\approx$Pluronic-L64. Of the polymers tested, only ABS with PEG-2000 and PEG-3400 have a reasonable chance for successful implementation using traditional solvent extraction apparatus.

Phase diagrams for the five ABS studied are presented in Fig. 2. The three PEG systems show the anticipated behavior with the binodals shifted to lower salt concentrations as polymer molecular mass increases. (It takes less $(NH_4)_2SO_4$ to salt-out PEG-
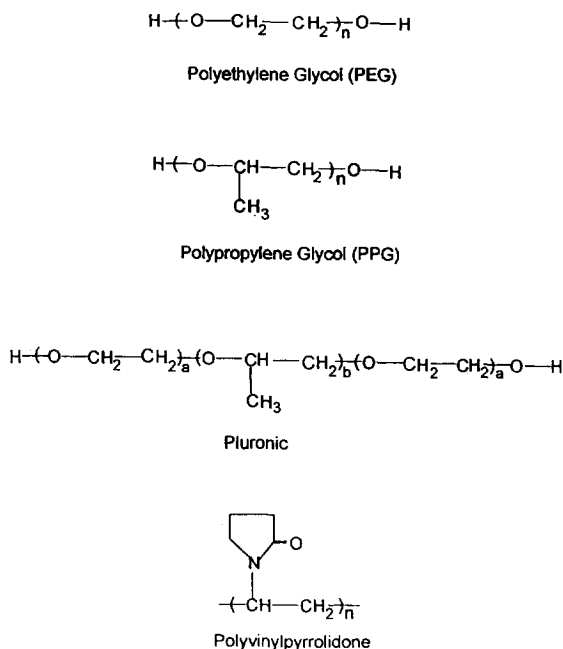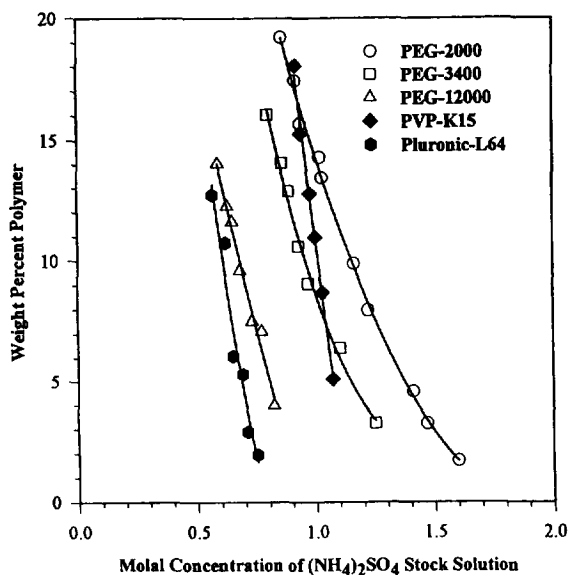


Fig. 1. Polymers used in this study.



Fig. 2. Phase diagrams for the five ABS determined by turbidimetric titration [23].

12 000 than PEG-3400.) The binodal for PVP-K15, which has an average molecular mass of $\approx 10\,000$, resides between that of PEG-2000 and PEG-3400. The binodal for Pluronic-L64 (molecular mass $\approx 2900$) is in the region of lowest polymer and salt concentrations, indicative of its increased hydrophobicity. In previous investigations into the partitioning of $TcO_4^-$ in ABS, the distribution ratio has been higher in ABS with lower binodals due to increased phase incompatibility at a given polymer and salt concentration. Based upon Fig. 2 we would thus predict that $D_{Tc}$ would increase in the order PEG-2000 < PVP-K15 < PEG-3400 < PEG-12 000 < Pluronic-L64.

Pertechnetate, although water soluble to a degree, is a fairly large polarizable molecule, and thus chaotropic. As a chaotropic ion, it prefers the polymer-rich phase over the highly structured salt-rich phase in a PEG-ABS. It has been demonstrated that as phase incompatibility increases, distribution of a solute will increase in the direction of preference [7,9,10,13–15]. Thus, by increasing salt or polymer concentration, we can increase $D_{Tc}$.

The distribution ratios obtained in this study are plotted in Fig. 3 as $D_{Tc}$ versus the molal concentration of $(NH_4)_2SO_4$ stock solution used to prepare the ABS with the given weight percent polymer stock solution. The PEG-like polymers follow the predicted trend in distribution ratios: PEG-2000 < PEG-3400 < PEG-12 000 < Pluronic-L64. Interestingly, however, the difference in $D_{Tc}$ for the PEG-3400 and PEG-12 000 ABS is minimal and not in keeping with the large difference in binodal position in Fig. 2. The $D_{Tc}$ values for the PEG-ABS appear to converge at high salt concentrations. Thus, there may be a practical limit on choice of polymer molecular mass with not enough of a gain in distribution ratio to offset the increased viscosity and expense of using higher molecular mass PEGs. We are currently investigating this possible convergence of distribution ratios for $TcO_4^-$, which may arise from a dehydration limit on the polymer-rich phase. That is, if too much water is excluded from the polymer-rich phase, this phase is too hydrophobic to support the pertechnetate ion as we observe for the PPG-2000 system.

The Pluronic-L64 gives the highest distribution ratios and it does so at a much lower polymer
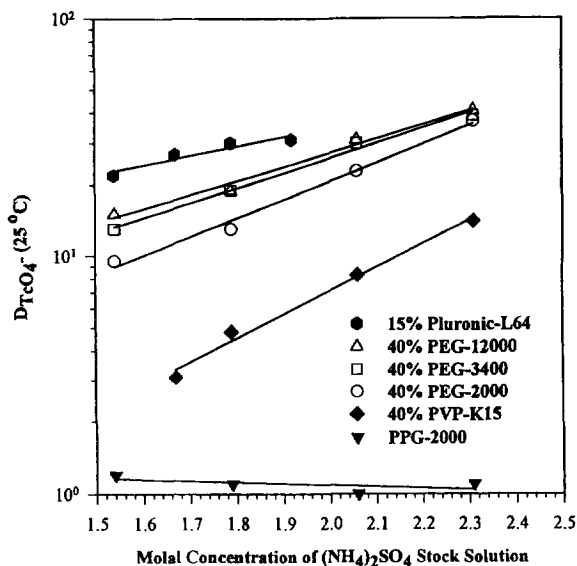


Fig. 3. Pertechnetate distribution ratios versus the molal concentration of $(NH_4)_2SO_4$ stock solution used to prepare the biphase with the indicated polymer stock solutions.

concentration. This observation is in keeping with its relative position in the phase diagram in Fig. 2. PVP-K15, on the other hand, exhibits much lower than anticipated $D$ values, and pertechnetate tends to evenly distribute between the phases in a PPG-2000–$(NH_4)_2SO_4$ system. Apparently, PPG-2000 is too hydrophobic, and thus the water content of this phase is too low, to provide $TcO_4^-$ with a suitable environment. This is in keeping with the distribution ratio of the salt anion [0.0054 in a 1.6 $M$ $(NH_4)_2SO_4$–PPG-2000 system] which indicates virtually no salt in the PPG phase.

Distribution ratios for the sulfate anion in ABS are higher than observed for the PPG system, since significant amounts of salt can reside in the polymer-rich phase. For the series of three PEG polymers, the sulfate distribution ratios follow from the positions of the binodals in Fig. 2 and are indicative of the increasing phase incompatibility created as polymer molecular mass increases. The distribution ratios for sulfate measured in a system prepared with equal aliquots of 40% polymer and 1.6 $M$ $(NH_4)_2SO_4$ are 0.31 (PEG-12 000), 0.52 (PEG-3400), 0.59 (PVP-K15), and 0.63 (PEG-2000). At a much lower
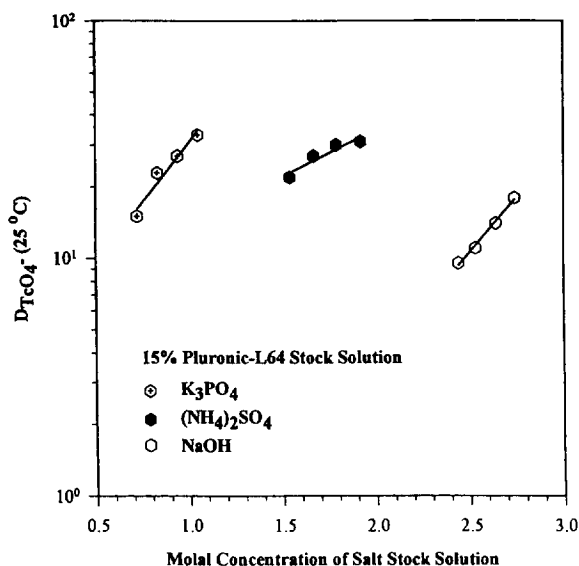
Fig. 4. Distribution ratios for pertechnetate in ABS prepared with 15% Pluronic-L64 and the indicated salt stock solutions.

Pluronic-L64 concentration of 15%, the distribution ratio measured for the sulfate ion was 0.63.

We have previously shown that the more negative the Gibbs free energy of hydration, the less salt is required to salt out PEG, and the higher the distribution ratios for pertechnetate will be at a given molal salt concentration [17]. The same is true for Pluronic-L64 as indicated in Fig. 4, although again, the useful range of salt concentrations is limited. ABS were successfully prepared with Pluronic-L64 and NaOH, $(NH_4)_2SO_4$, and $K_3PO_4$. The distribution ratios reflect both the increasing phase incompatibility in the order $OH^- < SO_4^{2-} < PO_4^{3-}$, and that generated as salt concentration increases.

## 4. Conclusions

Polymer hydrophobicity can be fine-tuned to increase phase incompatibility in ABS and thus increase distribution ratios of certain solutes. Thus Pluronic-L64 exhibits the highest $D_{Tc}$ values in this study, while there is virtually no separation of pertechnetate between the phases in the PPG-2000 system. The possible gain in distribution ratio, however, must be balanced against such performance

degrading physical characteristics as increased viscosity, increased phase disengagement times, and limited solubilities, as well as increased cost of custom polymers. In the present study, Pluronic-L64 was found to not be a suitable substitute for PEG-2000 despite the higher $D_{Tc}$ values at lower polymer concentrations. The versatility of PEG-2000 ABS (primarily the ability to use a wide range of salt concentrations) and the physical characteristics of the phases more than compensate for slightly lower distribution ratios. Nonetheless, we are currently investigating a wider range of Pluronic and other polymers to strengthen our understanding of the partitioning behavior of the pertechnetate anion and possibly to find more useful polymer-ABS.

## Acknowledgments

## References

[1] R.E. Boyd, Radiochim. Acta, 30 (1982) 123.
[2] J. Steigman and W.C. Eckelman, The Chemistry of Technetium in Medicine, National Academy Press, Washington, DC, 1992.
[3] M.L. Lamson III, A.S. Kirschner, C.E. Hotte, E.L. Lipsitz and R.D. Ice, J. Nucl. Med., 16 (1975) 639.
[4] A.G.C. Nair, S.K. Das, S.M. Desmukh and S. Prakash, Radiochim. Acta, 57 (1992) 29.
[5] G.J. Lumetta, B.M. Rapko, M.J. Wagner, C.D. Carlson and R.J. Barrington, Sludge Treatment and Extraction Technology Development: Results of FY 1993 Studies, Report PNL-9387, Pacific Northwest Laboratory, Richland, WA, 1994.
[6] J.L. Straalsund, J.L. Swanson, E.G. Baker, J.J. Holmes, E.O. Jones and W.L. Kuhn, Clean Option: An Alternative Strategy for Hanford Tank Waste Remediation. Volume 1. Overview, Report PNL-8388, Pacific Northwest Laboratory, Richland, WA, 1992.
[7] R.D. Rogers, A.H. Bond, C.B. Bauer, J. Zhang, M.L. Jezl, D.M. Roden, S.D. Rein and R.R. Chomko, in R.D. Rogers and M.A. Eiteman (Editors), Aqueous Biphasic Separations: Biomolecules to Metal Ions, Plenum Press, New York, 1995.
[8] R.D. Rogers, A.H. Bond and C.B. Bauer, Sep. Sci. Technol., 28 (1993) 1091.
[9] R.D. Rogers, J. Zhang, A.H. Bond, C.B. Bauer, M.L. Jezl and D.M. Roden, Solvent Extr. Ion Exch., 13 (1995) 665.

[10] R.D. Rogers, A.H. Bond, C.B. Bauer, J. Zhang, S.D. Rein, R.R. Chomko and D.M. Roden, Solvent Extr. Ion Exch., 13 (1995) 689.

[11] R.D. Rogers, A.H. Bond, J. Zhang and C.B. Bauer, Int. J. Appl. Rad. Isot., (1995) submitted.

[12] H. Walter, G. Johansson and D.E. Brooks, Anal. Biochem., 197 (1991) 1.

[13] M.A. Eiteman, J. Chromatogr. A, 668 (1994) 13.

[14] L.M. Cohen and J.L. Gainer, Sep. Sci. Technol., 29 (1994) 1925.

[15] M.A. Eiteman and J.L. Gainer, J. Chromatogr., 586 (1991) 341.

[16] Y. Marcus, J. Chem. Soc., Faraday Trans., 87 (1991) 2995.

[17] R.D. Rogers, A.H. Bond, C.B. Bauer, J. Zhang and S.T. Griffin, J. Chromatogr. B, 680 (1996) 221.

[18] P. Hubert in H. Walter and G. Johansson (Editors), Methods in Enzymology. Aqueous Two-Phase Systems, Vol. 228, Academic Press, San Diego, CA, 1994, p. 287.

[19] P. Linse, J. Phys. Chem., 97 (1993) 13896.

[20] G. Fleischer, J. Phys. Chem., 97 (1993) 517.

[21] P. Linse, Macromolecules, 26 (1993) 4437.

[22] P.A. Alred, F. Tjerneld, A. Kozlowski and J.M. Harris, Bioseparation, 2 (1992) 363.

[23] P.-Å. Albertsson, Partition of Cell Particles and Macromolecules, John Wiley, New York, 3rd ed., 1986.