

Research

MOLECULAR DYNAMIC SIMULATIONS IN DIGLYCOLAMIDES –Eu(NO₃)₃ SYSTEM**A.S. Suneesh, K.A. Venkatesan*, M.P. Antony, P. R. Vasudeva Rao****Fuel Chemistry Division, Indira Gandhi Centre for Atomic Research, Kalpakkam - 603 102. India.****Received date:** 20-12-2015; **Accepted date:** 26-02-2016; **Published date:** 15-03-2016**CORRESPONDENCE AUTHOR:** K. A. Venkatesan**E-mail:** kavenkat@igcar.gov.in**CONFLICTS OF INTEREST**

There are no conflicts of interest for any of the authors.

ABSTRACT:

Alkyl diglycolamides (DGAs) are promising extractants for the separation of trivalent actinides from nitric acid medium. Molecular dynamic simulations using AMBER force field have been performed on various alkyl derivatives diglycolamides to understand the fundamental property and conformation of DGA responsible for extraction of trivalent metal ions. Since the amidic (O1 and O2) and etheric oxygen donor atoms in DGA molecule coordinates with metal ions, the linear distance between O1-O3 atoms and the dihedral angle associated with O1-C1-C2-O2 and O2-C3-C4-O3 bonds present in DGAs were determined by MD simulations. The results obtained were correlated to the distribution ratio of americium (III). The average O1-O3 distance increased with increase of chain length and branching of alkyl group attached to amidic nitrogen atom of DGA. The extractant underwent remarkable change in conformation, prior to coordination with metal ions, to adopt a suitable conformation necessary for efficient complexation. Comparison of the results obtained from simulation and distribution ratios, our studies revealed that diglycolamides required an optimum O1 –O3 distance of 4.2 -5 Å and minimal reorientation of dihedral angles for efficient coordination with trivalent metal ions.

KEY WORDS: Molecular dynamics, AMBER force field, Diglycolamide, Solvent extraction, Europium.**INTRODUCTION**

Partitioning of trivalent actinides (Am(III), Cm(III)) from high-level nuclear waste and transmutation of them in advanced fast reactors is essential for the safe-management of nuclear waste. Partitioning is generally carried out by the actinide specific extractants such as carbamoylorganophosphorous compounds (TRUEX process) [1-2], diamides (DIAMEX process) [4,5], trialkylphosphine oxides (TRPO process) [6,7] and diisodecylphosphoric acid (DIDPA) [8,9] etc. In the recent past, alkyl derivatives of diglycolamides (DGA) are regarded as promising candidates for the separation of trivalent actinides from high-level liquid waste [10,11]. The structure of DGA is represented in figure 1. The presence of an etheric oxygen between the two amidic groups in DGAs, increases the extraction of minor actinides due to enhanced tridentate complex formation with trivalents.

Depending upon the alkyl group attached to the amidic nitrogen atom, the DGA is classified in to symmetrical, if the alkyl groups are same (R1 = R2, figure 1), and unsymmetrical DGA if R1 and R2 are different. The studies carried out so far on diglycolamides indicate that the extraction and stripping of trivalents, as well as the hydrodynamic and the tendency towards third phase formation are strongly dependent on the structure and properties of alkyl group attached to the amidic nitrogen atom [12]. Third-phase formation is an undesirable event namely the splitting of organic phase into two phases during the course of solvent extraction [13]. The recent studies on unsymmetrical diglycolamides [14] indicate that by proper selection of alkyl groups attached to amidic nitrogen atom, the extractive properties and third phase formation behavior can be tuned. Therefore,

it is imperative to investigate the fundamental property of diglycolamide that governs the extraction behavior.

Molecular dynamic simulations have been extensively employed for understanding the conformations of organic molecules and insights of solvent extraction [15-18]. Molecular mechanics offers several advantages over the quantum approach when dealing with bigger molecules and in simulating the solvent extraction phenomenon. Hirata et al. [18] studied structural stability of Eu^{3+} and UO_2^{2+} DGA complexes in vacuum, aqueous and in methanol phase. The authors reported that the Eu^{3+} -DGA complex was dissociated in water, however, the complex was stable in methanol and it was attributed to the selectivity of the trivalent cation as complex to UO_2^{2+} . Charbonnel et al. [19] studied the speciation of some lanthanide (III) and water soluble tetraethyldiglycolamide (TEDGA). The simulations confirmed that nitrate counter ions never enter in the inner sphere of the complex in aqueous solution water solution and that the stability of the complex was dependent on the a function of the competition between water and TEDGA coordination toward the Ln(III) cation.

In this paper, we report the results of MD simulations performed on some diglycolamides using AMBER force field to understand the extraction behavior of various alkyl substituted DGAs. The alkyl group attached to the amidic nitrogen atom was varied from octyl to dodecyl moiety. The distance between the two amidic oxygens (O1-O3) and the dihedral angle between the amidic and etheric oxygen (O1-C1-C2-O2 and O2-C3-C4-O3) were computed and correlated to the distribution ratio of americium in those DGAs. The conformation of DGA obtained in vacuum was compared with $\text{Eu}(\text{NO}_3)_3$ -DGA complex.

EXPERIMENTAL

2.1 Computational methods

All the molecular dynamics simulations and energy minimization calculations were performed in vacuum using the Assisted Model Building with Energy Refinement-11.0 (AMBER-11.0) package [20]. The Generalized Amber force-field (GAFF) corresponding to equation 1 was employed in the present study and the significance of each term is described elsewhere [21]. The force field parameters for Eu^{3+} were generated by using the input parameters reported by Wipff et al. [22]. The input parameters for energy minimization (.pdb files) were generated in chemsketch-12.0 [23] with the help of Avagadro package [24]. The trajectories of the structures were visualized by Visual Molecular Dynamics (VMD) package [25].

$$E_{\text{pot}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_\theta (\theta - \theta_{\text{eq}})^2 + \sum_{\text{dihedrals}} \sum_n V_n (1 + \cos(n\phi - \gamma)) + \sum_{i < j} \left[\epsilon_{ij} \left(\left(\frac{R}{R_{ij}} \right)^{12} - \left(\frac{R}{R_{ij}} \right)^6 \right) \right] + \sum_{i < j} \left[\frac{q_i q_j}{R_{ij}} \right] \sum_{\text{H-bonds}} \left[\epsilon_{ij} \left(\left(\frac{R}{R_{ij}} \right)^{12} - \left(\frac{R}{R_{ij}} \right)^{10} \right) \right] \quad (1)$$

2.2 Energy minimization

Energy minimizations were performed to optimize the equilibrium structure corresponding to nearest local minimum, by carrying out geometric corrections. During energy minimization, the molecules re-orient only with respect to its local environment. Energy minimization was performed for 10000000 cycles using a non-bonded cut-off 12 Å by constant volume periodic boundary conditions. In the present study, the minimization was performed by steepest descent method for 500000 cycles and then conjugate gradient method was switched on. An out-put file was written as coordinate information corresponding to each cycles.

2.3 Molecular dynamics simulations

The geometry optimized structures obtained by using energy minimization were subjected to N-body motion at a reference temperature (300 K) during molecular dynamics simulation. In molecular dynamic simulations the atoms and molecules are allowed to interact over a period of time and the forces between these particles are monitored as a function of time. The MD simulations are performed by using the energy minimized coordinates by applying a non-bonded cut-off 12 Å, at a temperature of 300 K. The temperature scaling were performed by using a constant temperature canonical ensemble, with the help of Langevin dynamics with a constant collision frequency of 5 ps⁻¹. Constant volume periodic boundary conditions were applied for the MD simulations. Though, the temperature is assumed to be 300 K, it may change slightly during the course of simulations, due to rapid collisions of the molecules, as a result the kinetic energy also varies as a function of time. In the present study, the temperature, energy and coordinate informations were recorded at every 1000 steps of the total MD simulations reference-time scale.

2.4 Time evolution plots

The results of molecular dynamics simulations were monitored by the changes in the parameters such as O1-O3 distance and the dihedral angles corresponding to O1C1C2O2 and O2C3C4O3. These parameters were calculated by using a simple algorithm generated for finding out the these distances and dihedral angles from the coordinates generated at various time-steps. These values were generated as separate files during the period of simulations.

2.5 Population distribution plots

When molecular collisions are switched on by applying temperature, it undergoes various changes in the structure and energy. Each molecule re-orient its geometry in accordance with its neighbors. Therefore, the bond angles and equilibrium distances of various atoms for example O1-O3 distance changed over a period time, leading to the distribution of various conformations. Populations of various O1-O3 distances and O1C1C2O2 and O2C3C4O3 dihedral angles were calculated from the distribution data obtained from the time evolution informations.

RESULTS AND DISCUSSIONS

The DGAs investigated in the present study have different alkyl substituents. The nature of substituents attached to the amidic nitrogen atom and their abbreviations are shown in table 1. The distribution ratio of Am(III) reported for these DGAs are also shown in table 1. It is observed that the distribution ratio of Am(III) in 0.1 M DGA/n-DD is dependent on the nature of alkyl group attached. For instance, the diglycolamides such as C8-C8, C8-C8' and C8'-C8' are chain isomers, differing only in the structure of alkyl group attached to the amidic nitrogen atom. However, the distribution ratios obtained in those systems are remarkably different and it decreases with increase of branching of alkyl group in the order C8-C8 > C8-C8' > C8'-C8'. Similarly, the distribution ratio of Am(III) decreases with increase of chain length of alkyl group attached to the amidic nitrogen atom of DGA in the order C8-C8 > C10-C10 > C12-C12. This indicates that the alkyl group attached to the amidic nitrogen atom plays a profound role in determining the distribution ratios, even though the co-ordinating site is oxygen in all DGAs. This shows it is quite likely that the alkyl group attached to the amidic nitrogen would be deciding the conformation responsible for the formation of stable Am(III)-DGA complex and therefore, their distribution ratios. To understand the conformational

behavior of DGAs and metal-DGA complex, MD simulations were performed and the results are discussed below. Since the AMBER force field for Am(NO₃)₃ was not available in literature, Eu(NO₃)₃ was employed for simulation in the present study as the extractive properties of Am(III) and trivalent lanthanides were quite similar [22]. Therefore, the distribution ratio trend observed for Am(III) and Eu(III) were similar.

Table 1. DGAs investigated in the present study and the

Abbreviation	Alkyl substituent on amidic nitrogen atom		D _{Am(III)} [References in parenthesis]
	R1	R2	
C8-C8	Octyl	Octyl	24 [26]
C10-C10	Decyl	Decyl	10 [27]
C12-C12	Dodecyl	Dodecyl	6 [27]
C8-C8'	octyl	2-Ethylhexyl	2.3 [14]
C8'-C8'	2-Ethylhexyl	2-Ethylhexyl	0.2 [28]

distribution ratio of Am(III) in 0.1 M DGA/n-dodecane from 1.0 M nitric acid at 298 K

It is well-recognized that extraction of Eu(III) by diglycolamides results in the formation of co-ordinate complex of Eu(NO₃)₃ with DGA through oxygen donor atoms. Therefore, it is necessary to understand the changes that could occur in O1-O3 distance, and dihedral angles associated with O1-C-C-O2 and O2-C-C-O3 bonds in DGAs upon changing the nature of alkyl substitutes (figure 1). Therefore, molecular dynamic simulation was performed to determine the linear distance between the O1-O3 atoms of DGA to understand the effect of alkyl substitutes. During MD simulations, the molecule undergoes various kinds of conformational changes before reaching a stable conformation at equilibrium. The time evolution plot for the attainment of equilibrium conformation is shown in figure 2. The MD simulation was performed for 100 ns. It is observed that the molecule achieves

equilibrium in 10 ns. After 10 ns, the changes in conformations are insignificant there after.

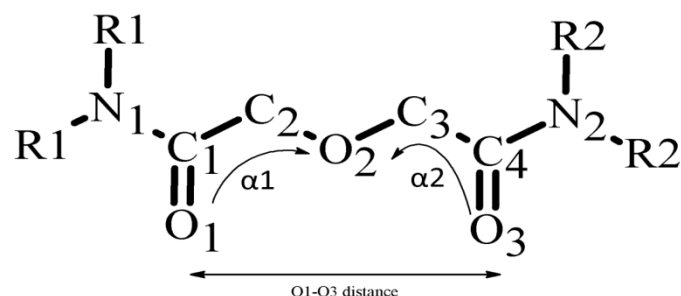


Figure 1. Alkyl derivatives of diglycolamide indicating O1-O3 distance and dihedral angles α_1 and α_2 . $R_1=R_2$ is Symmetrical DGA, $R_1 \neq R_2$ is Unsymmetrical DGA.

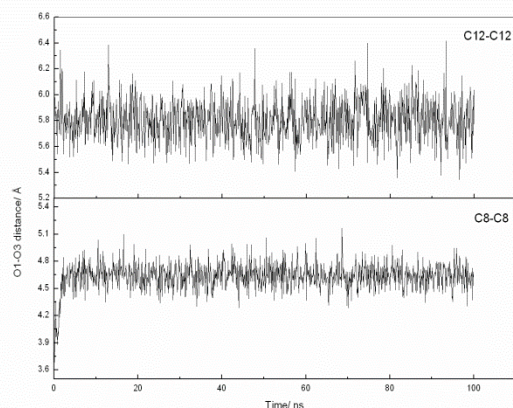


Figure 2. Time evolution of O1-O3 distance of C8-C8 and C12-C12

The conformations obtained from 10 ns to 100 ns were recorded and the O1-O3 distance was determined in the last ~1000 conformations, which were obtained after establishing equilibrium. The results indicate that O1-O3 distance measured in vacuum for DGAs is distributed over various O1-O3 distances as shown in figure 3. It is observed that the average linear distance increases with increase in chain length of alkyl group attached to amidic nitrogen in the order C8-C8 < C10-C10 < C12-C12. These results are exactly opposite to the distribution ratio order observed for Am(III) extraction, which decreases in the order C8-C8 > C10-C10 > C12-C12. Figure 3 also shows the distribution of O1-O3 distance measured for various diglycolamides in the presence of $\text{Eu}(\text{NO}_3)_3$ and nitric acid. Similar to the previous case obtained in vacuum, the O1-O3 distance increases with increase in the chain length of alkyl group attached to amidic nitrogen in the order C8-C8 < C10-C10 < C12-C12. Since the distribution ratio reported for C8-C8 is higher than other DGAs and comparing the results observed in

figure 3 with distribution ratios in table 1, the study shows that diglycolamides seem to require an optimum O1-O3 distance of 4.2 to 5 Å for efficient coordination. Any deviation from this optimum value could result in decrease of distribution ratio. Kannan et al [29] studied the single crystal structure of $\text{La}(\text{NO}_3)_3\text{-C}_8\text{-C}_8$ complex. It was reported that the O1-O3 distance in the complex was 4.35 Å, which was in good agreement with the simulated values of 4.2 to 5 Å obtained, in the present study.

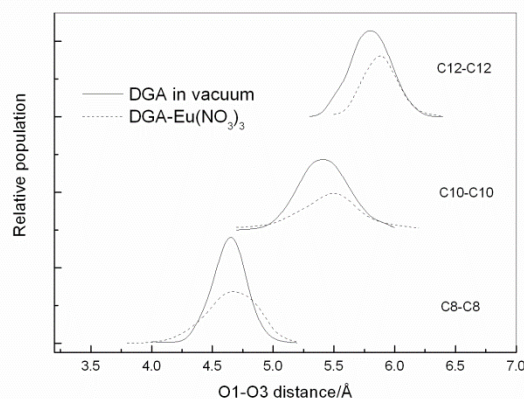


Figure 3. Variation in the distribution of O1-O3 distance in DGAs as a function of alkyl chain length.

The results on the O1-O3 distances determined for isomeric diglycolamides containing the octyl moiety is shown in figure 4. It is observed that the average O1-O3 distance increases upon branching of alkyl group attached to the amidic nitrogen atom. Comparing these observations with the distribution ratio of Am(III) tabulated in table 1, the study confirms that the deviation from the optimum O1-O3 distance of 4.2 to 5 Å results in lowering of distribution ratio. When the simulation was carried out in the presence of $\text{Eu}(\text{NO}_3)_3$ the O1-O3 distance is distributed in the region of that obtained in vacuum only in case of C8-C8 and C8-C8'. This indicates that the changes in the O1-O3 distance upon complexation with $\text{Eu}(\text{NO}_3)_3$ is insignificant. However, the O1-O3 distance is shifted to some extent from 5.8 Å to 5.2 Å in case of C8'-C8' upon complexation with Eu(III). This shows that the diglycolamide, C8'-C8', undergoes reorientation of molecule to some extent to adopt a specific conformation for complexing with $\text{Eu}(\text{NO}_3)_3$. Since this kind of reorientation involve strain in the molecule, the distribution ratio of Am(III) observed in C8'-C8' is quite low as compared to other isomeric diglycolamides.

Reorientation of DGA molecule can be verified by the examining the dihedral angle of O1-C-C-O2 (α_1) and O2-C-C-O3 (α_2) bonds (figure 1) in

DGAs determined in vacuum and in $\text{Eu}(\text{NO}_3)_3$ complex. The dihedral angle α can have any value from 0° to 360° as shown in figure 1. Figure 5 shows the comparison of dihedral angles determined for some DGAs in vacuum and in $\text{Eu}(\text{NO}_3)_3$ complex. Similar to the O1-O3 distance, the dihedral angle is distributed over various values. It is observed that the change in dihedral angle upon complexation with $\text{Eu}(\text{NO}_3)_3$ is insignificant in case of C8-C8. This indicates that this diglycolamide can form a complex with $\text{Eu}(\text{III})$ without much reorientation of bonds and bond angles. Higher distribution ratio obtained for C8-C8 also comprehends well with this observation. For other diglycolamides, shown in figure 5, the dihedral angle changes to different value for complexation with $\text{Eu}(\text{NO}_3)_3$. Since this kind of reorientation involves strain in the molecule, the distribution ratios observed for other DGAs are less.

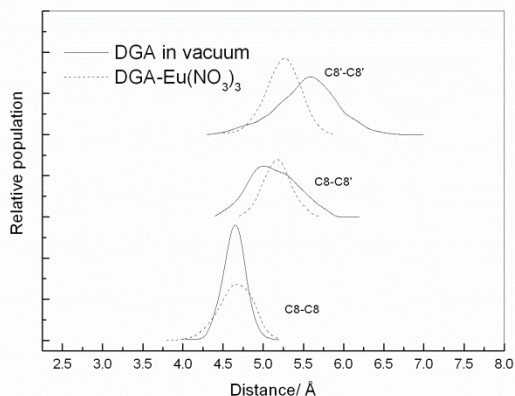


Figure 4. Variation in the distribution of O1-O3 distance in DGAs as a function of alkyl chain length.

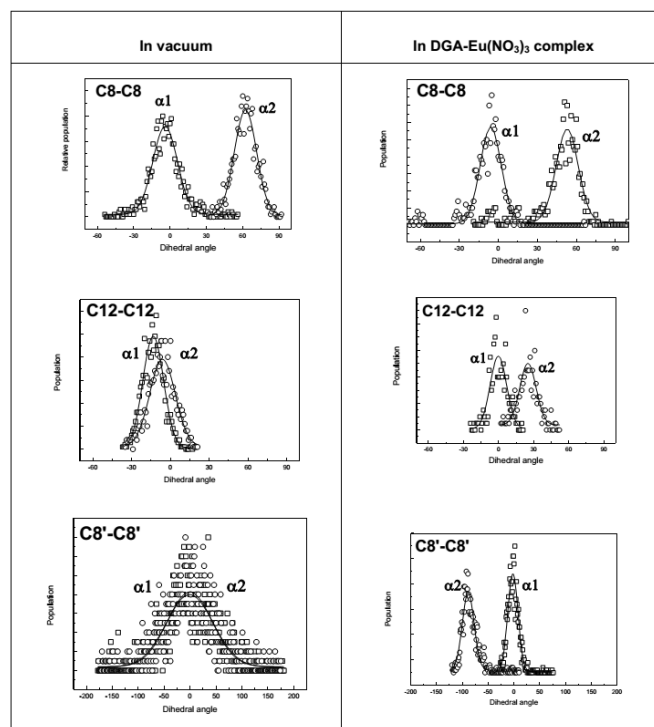


Figure 5. Population distribution of O1-C1-C2-O2 and O2-C3-C4-O3 as function of alkyl chain length

CONCLUSIONS

Molecular dynamic simulation was performed on some diglycolamides containing different alkyl groups. The spatial arrangement of the two amidic oxygen atoms (O1-O3) and the dihedral angles O1-C-C-O2 (α_1) and O2-C-C-O3 (α_2) bonds in DGAs were determined in vacuum and in $\text{Eu}(\text{NO}_3)_3$ complex. The distances thus obtained were correlated to the distribution ratio of americium (III). The average linear O1-O3 distance increased with increase in chain length in the order C8-C8 < C10-C10 < C12-C12 and with branching in the order C8-C8 < C8'-C8' < C8'-C8'. The diglycolamides required an optimum O1-O3 distance of 4.2 to 5 Å for efficient coordination with trivalent metal ions. Any deviation from this optimum value required reorientation of the molecule to adopt a suitable conformation for coordinating with metal ion. Such reorientation seems to result in strain in the molecule and thus lowers the distribution ratio of Am(III).

References

1. Mathur JN, Murali MS, Nash KL, Actinide partitioning—A review, *Solvent Extr. Ion Exch.* 19: 357-362, 2001.
<https://www.researchgate.net/publication/255945912>
2. Schulz WW, Horwitz EP, The TRUEX process and the management of liquid TRU waste. *Sep. Sci. Technol.* 23, 1191-1201: 1998.

- <https://www.researchgate.net/publication/244610520>
3. Ansari SA, Pathak PN, Mohapatra PK, Manchanda VK, Aqueous partitioning of minor actinides by different processes, *Sep. Purif. Rev.* 40, 43-53: 2011.
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2958570/>
 4. Modolo G, Amato L, Modolo G, Nannicini R, Madic C, Baron P, DIAMEX counter-current Extraction process for recovery of trivalent actinides from simulated High active concentrate, *Sep. Sci. Technol.* 42,439-452:2007.
<http://publications.jrc.ec.europa.eu/repository/handle/JRC41098>
 5. Berthon L, Morel JM, Zorz N, Nicol C, Virelizier H, Madic C, DIAMEX process for minor actinide partitioning: Hydrolytic and radiolytic degradation of malonamide extractants, *Sep. Sci. Technol.* 36,709-728:2001.
 6. Liu X, Liang J, Xu J, Simplified Chinese TRPO process to Extract and recover Transuranium elements from High-level liquid waste. *Solvent Extr. Ion Exch.* 22,163-173:2004.
<http://www.tandfonline.com/doi/abs/10.1081/S-EL-120030393>
 7. Jianchen W, Chongli S, Hot test of Trialkyl phosphine oxide(TRPO) for removing actinides from Highly saline High-level liquid waste (HLLW), *Solvent Extr. Ion Exch.* 19,231-242:2001.
<http://www.tandfonline.com/doi/abs/10.1081/S-EL-100102693?journalCode=lsej20#.V10TWTVuFXU>
 8. Morita Y, Glatz JP, Kubota M, Koch L, Pagliosa G, Roemer K, Nicholl A, Actinide Partitioning from HLW in a continuous DIDPA extraction process by means of centrifugal extractors. *Solvent Extr. Ion Exch.* 14,385-400:1996.
<http://www.tandfonline.com/doi/abs/10.1080/07366299608918346?journalCode=lsej20#.V10TdT YuFXU>
 9. Nakamura S, Akiba K, Transport of Europium(III) through supported liquid membrane containing diisodecylphosphoric acid, 24,673-686:1989.
<http://www.ncbi.nlm.nih.gov/pubmed/18968464>
 10. Ansari SA, Pathak PN, Manchanda VK, Hussain M, Prasad AK, Parmar VS, N,N,N',N'-Tetraoctyl Diglycolamide (TODGA), A promising extractant for actinide –partitioning from high-level waste (HLW), *Solvent Extr. Ion Exch.* 23,463 –479:2005.
 11. Magnusson D, Christiansen B, Glatz JP, Malmeck R, Modolo G, Purroy DS, Sorel C, Demonstration of a TODGA based extraction process for the partitioning of minor actinides from a PUREX raffinate, *Solvent Extr. Ion Exch.* 27,26-35:2009.
 12. Ansari SA, Pathak PN, Mohapatra PK, Manchanda VK, Chemistry of diglycolamides: promising extractants for actinide partitioning, *Chem. Rev.* 112,751–1772:2012.
 13. Vasudeva Rao PR, Kolarik Z, A review of third phase formation in extraction of actinides by neutral organophosphorus extractants, *Solvent Extr. Ion Exch.* 14,955-993:1996.
 14. Ravi J, Venkatesan KA, Antony MP, Srinivasan TG, Vasudeva Rao PR, Tuning the diglycolamides for modifier-free minor actinide partitioning, *J. Radioanal. Nucl. Chem.* 295,1283-1292:2012.
 15. Beudaert P, Lamare, V, Dozol JF, Troxler L, Wipff G, Theoretical studies on tri-n-butyl phosphate: md simulations in vacuo, in water, in chloroform, and at a water / chloroform interface, *Solvent Extr. Ion Exch.* 16,597 – 618:1996.
 16. Suneesh AS, Ashok Kumar GVS, Gururaj K, Venkatesan KA, Valsa Kumar MC, Vasudeva Rao PR, Conformational and coalescence behaviour of trialkylphosphates in vacuum, water and dodecane, *J. Mol. Model.* 20, 1-8:2014.
 17. Zheng H, Wu F, Wang B, Wu Y, Molecular dynamics simulation on the interfacial features of phenol extraction by TBP/dodecane in water, *Comput. Theor. Chem.* 970,66-72:2011.
 18. Hirata M, Guilbaud P, Dobler M, Tachimori S, Molecular dynamics simulations for the complexation of Ln³⁺ and UO₂²⁺ ions with tridentate ligand diglycolamide (DGA). *Phys. Chem. Chem. Phys.* 5,691-695:2003.
 19. Charbonnel MC, Berthon C, Berthon L., Boubals N, Burdet F, Duchesne MT, Guilbaud P, Mabilhe N, Petit S, Zorz N, Complexation of Ln(III) and Am(III) with the hydrosoluble TEDGA: speciation and thermodynamics studies. *Procedia Chem.* 7,20–26:2012.
 20. AMBER-11 manual, <http://ambermd.org/>
 21. Özpınar, GA, Peukert W, Clark T, An improved generalized AMBER force field (GAFF) for urea. *J. Mol. Model.* 16,1427-1440:2010.
 22. Baaden M, Berny F, Wipff G, Madic C, A molecular dynamics and quantum mechanics study of M³⁺ lanthanide cation solvation by acetonitrile: the role of cation size, counterions and polarization effects investigated. *J. Phys. Chem. A* 104,7659-7671:2000.
 23. ChemsSketch-12.0,
<http://www.acdlabs.com/resources/freeware/chemsSketch/>
 24. Avagadro package, <http://www.avogadro.openmolecules.net/>

25. Humphrey W, Dalke A, Schulten K, Visual Molecular Dynamics, *J. Molec. Graphics* 14, 33-38:1996.
26. Ansari SA, Pathak PN, Manchanda VK, Hussain M, Prasad AK, Parmar VS, N,N,N',N',-tetraoctyldiglycolamide (TODGA):a promising extractant for actinide-partitioning from high-level waste (HLW), *Solvent Extr. Ion Exch.* 23,463-479:2005.
27. Sasaki Y, Sugo Y, Suzuki S, Shoichi S, The novel extractants, diglycolamides, for the extraction of lanthanides and actinides in HNO₃-n-dodecane system, *Solvent Extr. Ion Exch.* 19,91-103:2001.
28. Nayak PK, Kumaresan R, Venkatesan KA, Rajeswari S, Subramanian GGS, Antony MP, Vasudeva Rao PR, Single-cycle separation of americium (III) from simulated high-level liquid waste using tetra-bis(2-ethylhexyl)diglycolamide and bis(2-ethylhexyl)phosphoric acid solution, *J. Environ. Chem. Eng.* 1, 559-565:2013.
29. Kannan S, Moody MA, Barnes CL, Duval PB, Lanthanum(III) and uranyl(VI) diglycolamide complexes: synthetic precursors and structural studies involving nitrate complexation, *Inorg. Chem.* 47,4691-4695:2011.