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Azarbaijan Shahid Madani University

Investigation of Menthol and Caprylic acid based Deep Eutectic Solvent from the Point of View of Molecular Dynamics Simulation and COSMO-RS

Samaneh Barani Pour[1], Nasrin Jabbarvand Behrooz[2], Jaber Jahanbin Sardroodi[3*], Alireza Rastkar Ebrahimzadeh[4], Mohammad Sadegh Avestan[5]

[1,2,3,4]Molecular Science and Engineering Research Group (MSERG), Molecular Simulation Lab, Azarbaijan Shahid Madani University, Tabriz, Iran

[1]samaneh.barani90@gmail.com, [2]njabbarvand@yahoo.com, [3]jsardroodi@azaruniv.ac.ir, [4]a.rastkar110@gmail.com

[5]Department of Chemistry, University of Cincinnati, Cincinnati, OH 45221, United States

[5]avestamh@mail.uc.edu

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Abstract

The widespread use of toxic and volatile organic solvents has led to a new challenge in the industry. In this regard, the design of green and biodegradable solvents such as deep eutectic solvents (DESs) has attracted a lot of attention. Molecular-level description of the interactions between HBA and HBA can provide a valuable perspective for the design of these green solvents. In order to, COSMO-RS was used for screening potential DESs qualitatively. Then, we herein performed molecular dynamics (MD) simulations on DES based on Caprylic acid (CAP) and menthol (MEN) which is very widely used in the process of separating pollutants and biomolecules from the water environment and it was observed that the hydroxyl group of menthol plays a key role in the formation of deep eutectic solvents based on MEN and CAP.

Keywords: DESs, MD, Spatial distribution function, Mean-Square Displacement, Caprylic acid, Menthol

* Corresponding Author

Introduction

With the increasing expansion of the separation process using toxic and volatile organic solvents that produce a major part of dangerous air-polluting gases, green technology is seriously seeking to find suitable alternatives for these solvents in order to preserve the environment and reduce possible negative effects on human health. In this regard, ionic liquids (ILs) were used to replace these solvents [1]. Among the problems that exist in the use of ionic liquids is the high price of these compounds, so to overcome the high cost, new compounds called deep eutectic solvents (DESs), which have properties similar to ionic liquids, have recently attracted the attention of researchers [2].

Deep eutectic solvents are binary mixtures where the lack of charge stabilization through hydrogen bonding between the two hydrogen bond donor and acceptor components has led to a decrease in the melting point of this mixture compared to the pure components [3]. The most common DESs are based on choline chloride as a hydrogen bond acceptor, and carboxylic acids, citric acid, sugars, and other hydrogen bond donors such as urea and glycerol. DESs are very cheap, biodegradable, and non-toxic, which can be widely used in pharmaceutical and extraction industries.

A quick look at the DESs presented in the literature shows that the majority of these solvents are very hydrophilic. Recently, the chemical instability of hydrophilic solvents based on ammonium salts when in contact with water has motivated the design of hydrophobic DESs as green alternatives for organic solvents have doubled [4]. Hydrophobic DESs based on menthol and fatty acids are widely used in extracting biomolecules and pollutants from aqueous environments [5]. In this work the dynamical and structural properties of a DES composed of menthol and Caprylic acid were investigated through MD simulations at 298.15 K and the capability of menthol and Caprylic acid components in forming an acceptable DES was analyzed. Dynamical parameters such as mean square displacement (MSD), are calculated at the pressure of atmosphere. Structural parameters such as hydrogen bonds (H-bonds), radial and spatial distribution functions (RDF and SDF) were investigated. Also, for additional investigations of local polarization charge-density, sigma-profile determination analysis was performed in COSMO-RS.

Methodology

The methods of preparation and simulation of the binary mixture were as follows: first, the molecules (HBA and HBD) were designed using the Visual Molecular Dynamics (VMD) program [6]. The screening charge density distribution on the surface of HBA and HBD (σ-profile) was calculated using the COSMO-RS methodology. The COnductor-like Screening MOdel for Real Solvents (COSMO-RS) model is a thermodynamic model based on quantum chemistry and statistical thermodynamics that is useful for the preliminary design of DESs [7].

Then, the simulation box containing menthol ($C_{10}H_{20}O$) and Caprylic acid ($C_8H_{16}O_2$) molecules at a (1:1) molar ratio were prepared using PACKMOL software [8]. A periodic boundary condition was employed for the MD simulation. The valet algorithm is used with an integration time step of 1 for solving Newton's equations of motion. The MD simulations were performed for 50000 steps in NPT ensembles using the NAMD_2.13 package [9] at 298.15 K. Langevin thermostat [10] and Nose-Hoover thermostat [11] have been used to setting temperature and pressure, respectively. To investigate Long-range electrostatics, the particle mesh Ewald (PME) method with a 12 Å cutoff was considered.

To evaluate the equilibrium of the binary mixture, the root-mean-square deviation (RMSD) of species with respect to a reference structure was obtained, as defined in Equation 1.

$$RMSD = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - x_{i0})^2 + (y_i + y_{i0})^2(z_i + z_{i0})^2}$$

The results of Figure 1 show that the RMSD path increased at the beginning of the simulation, and then upon reaching convergence, the RMSD value for menthol and caprylic acid molecules reached constant values of 20.0 and 21.0, respectively (see Figure 1).

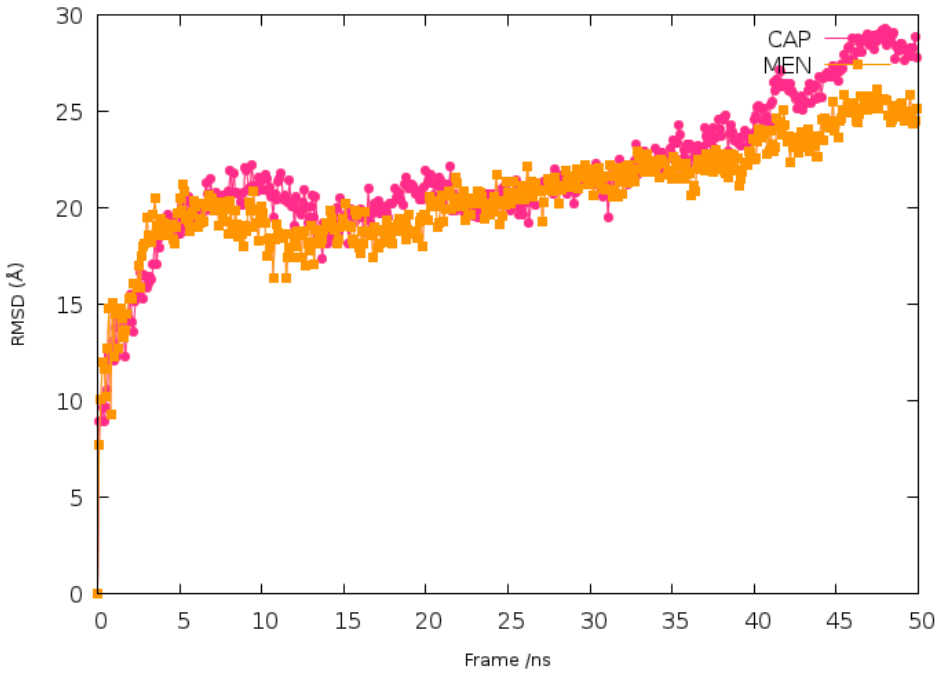

Figure. 1. Root mean square deviation (RMSD) analysis: RMSD of menthol and caprylic acid up to 50 ns

Results and discussion

To understand and identify the effective interactions in the formation of DES based on menthol and Caprylic acid, the structural properties of the binary mixture were investigated for the last 20 ns of the MD simulations.

RDF and Combined Distribution Functions

The radial distribution function is a useful quantity that represents the probability of finding a molecule at a distance r from another tagged molecule [12]. The radial distribution function is given by Equation (2),

$$g(r) = \frac{1}{\rho N} \langle \sum_{ij} \delta(r - r_{ij}) \rangle \quad (2)$$

,which N and ρ are the numbers of particles and number density, respectively.

To explore in detail the structural properties of the binary mixture, the strategy of site-site RDFs was used. The atomic sites of CAP (C, H, and O atoms) were selected and how to place them around the hydroxyl group of menthol (O1) was investigated in the binary mixture.

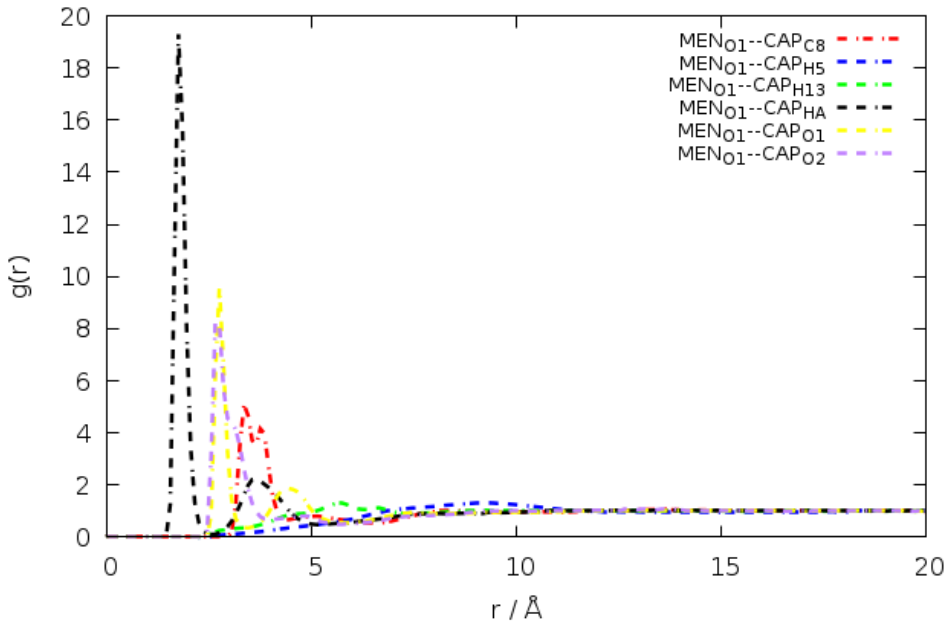

Figure 2. RDFs between different atoms of menthol and Caprylic acid molecules in the binary mixture at 323 K

The first maximum of peaks for the RDFs between the different atoms of HBD and the O atom of MEN located near 2 Å for the CA-HA···MEN.O pair, 3 Å for the CAP.O1(O2)···MEN.O pairs, 4 Å for the CAP-C8··· MEN.O pair. The sharp RDF peak indicates the H-bond interaction between the carboxyl group (C (=O) OH) of acid and menthol molecules. In Figure 3, the RDFs for the menthol --menthol, HBA --HBD pairs of the eutectic mixture at 298.15 K are shown. In addition, the first maximum of peak for $g(r)_{CAP-MEN}$ appears at closer intervals compared to the $g(r)_{MEN-MEN}$. It is likely that the hydrogen bonding interaction between HBA and HBD is significant in the mixture.

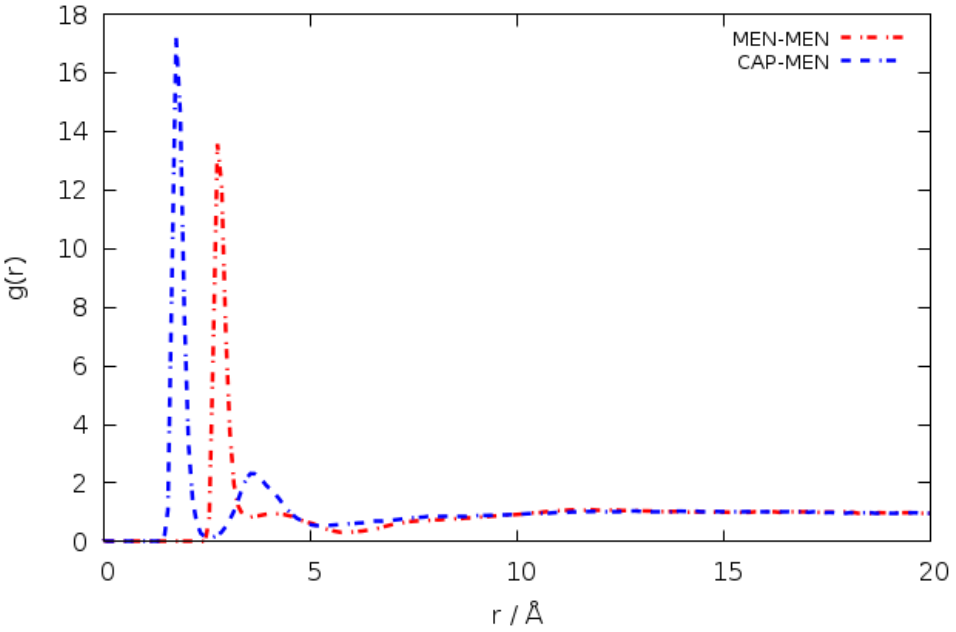

Figure. 3. RDFs between molecules in the binary mixture at 298.15 K

Hydrogen-Bond Analysis

Hydrogen bonding between HBA and HBD led to a decrease in the melting point of the eutectic mixture compared to the two separated components [13]. H-band distance and angle criteria were considered as follows: the A–H distance ~ 3.5 Å and the D–H–A angle ~150 degrees. The average H-bond between species can be evaluated as follows (well-known Gaussian distribution):

$$F(X) = \frac{a}{\sigma\sqrt{2\pi}} exp^{\frac{-(X-\bar{X})^2}{2\sigma^2}} \qquad (3)$$

$\bar{X}$ and σ are the average numbers of H-bond and standard deviation, respectively.

Observations show that the average H-bond between species was found to be in the order of CAP−MEN (0.18) > MEN−CAP (0.14). The hydrogen bonding results show a strong interaction between the HBA and HBD compared to the interaction between menthol molecules.

Occupancy analysis was performed to investigate the ratio of the number of hydrogen bonds between the possible HBD and HBA pairs [14]. The occupancy ratio of the CAP-MEN hydrogen bond was 99% in the mixture, whereas that of the MEN---MEN interaction was only 85%. It seems that the stability of the hydrogen bond between HBA and HBD is significant compared to hydrogen bonding between menthol molecules (Figure 5).

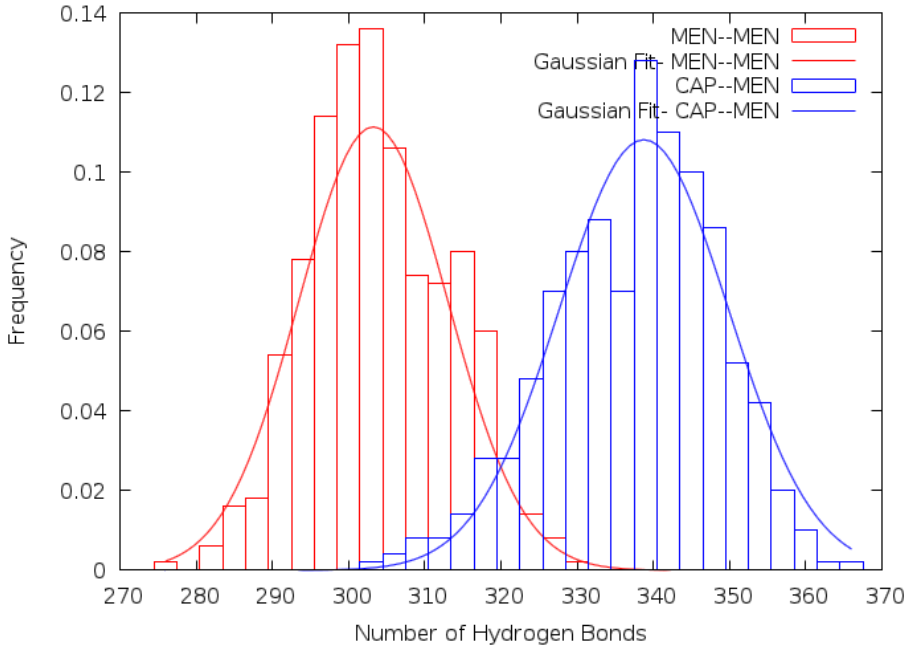

Figure. 4. The distribution of the H-bond number between MEN and CAP (and menthol molecules) in the binary mixtures at 298.15 K

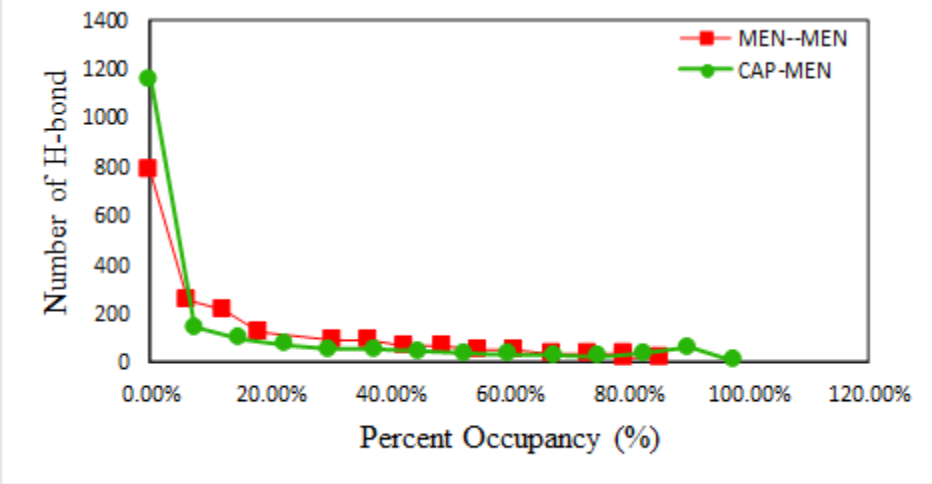

Figure 5. Hydrogen bond percent occupancies for MEN and CAP (MEN molecules) in the binary mixture at 310 K

Spatial distribution function (SDF)

To get a clearer picture of the 3D-arrangement and placement of the OH group of menthol around Caprylic acid and the acidic functional group of Caprylic acid around menthol, spatial distribution function (SDF) analysis for studying effective sites in intermolecular hydrogen-bond interactions [15] was evaluated with Travis package [16]. As can be seen from Figure 6 (a and b),

Caprylic acid is surrounded by the OH group of menthol with a condensed cup from the side of the acidic functional group, which indicates the presence of strong hydrogen bonds between the hydrogen and oxygen atoms of both components, and it can be said that the largest dense cap is related to menthol oxygen around Caprylic acid hydrogen atom, which confirms the narrow and sharp peak of menthol oxygen and Caprylic acid hydrogen at that distance in RDF.

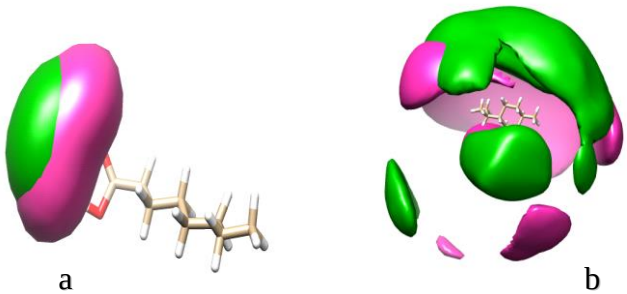

Figure 6. The SDF of (a) O--H of menthol (pink--green cap), around the Caprylic acid, and (b) the acidic functional group of Caprylic acid; HA (pink cap) around menthol

Mean-Square Displacement (MSD)

Because the transfer of molecules plays a vital role in determining the thermodynamic properties of solvents [17], for this purpose, the microscopic dynamics of the eutectic solvent under our study was investigated by the relation of the MSD and the relationship related to this quantity are as follows:

$$MSD = \langle |r_i(t) - r_i(0)|^2 \rangle = \frac{1}{N} \langle \sum_{i=1}^{N} \left| r_i^{COM}(t) - r_i^{COM}(0) \right|^2 \rangle \quad (4)$$

, which r_i (t) and r_i (0) are the positions of the i-th particle at time t and 0, respectively [18]. The MSDs of the center of mass of menthol and Caprylic acid species in the considered system are evaluated, as illustrated in Figure 7.

The MSD of menthol and Caprylic acid is compared as a function of time in Figure 7 and as it can be seen from the image, the lower slope of the MSD curve of the center of mass of menthol despite the low molecular mass of Caprylic acid can be attributed to lower mobility, and subsequently, the presence of the ring and the effective role of the OH group in establishing strong hydrogen bonds.

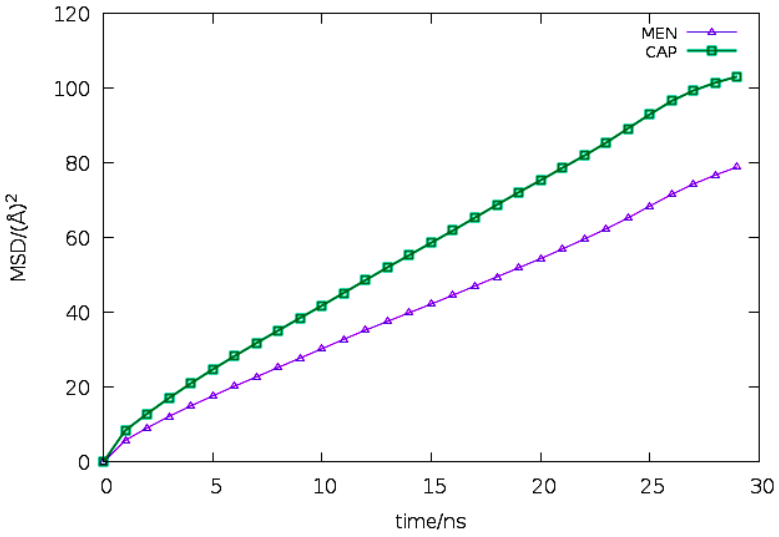

Figure 7. Comparison of the MSD of the center of mass of menthol and Caprylic acid species in the investigated DES

COSMO-RS- Sigma profiles

In order to quantitatively describe the surface of the molecule and considering that the surface interaction energies depend only on the local polarization charge-densities (the net composition of the surface of each component in the surface interactions of the local pair-wise) [19]. For this purpose, the sigma profiles of the components of the DES were evaluated and their diagrams are drawn in Figure 8. The COSMO-RS calculations

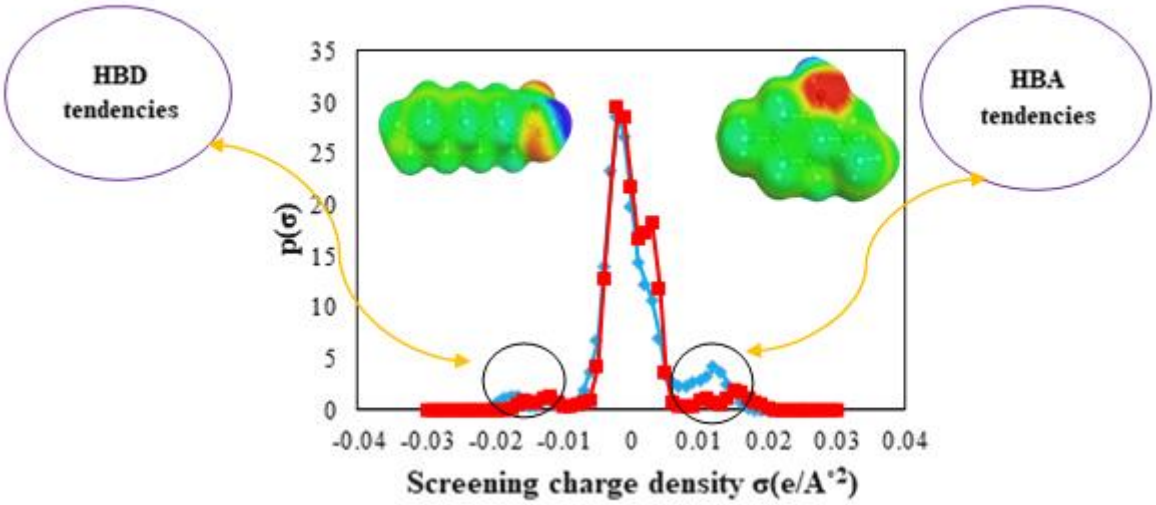

Figure 8. Sigma profiles of menthol (red), Caprylic acid (blue) and their sigma-surfaces representation

were carried out using the Turbomole software package (TmoleX version 4.2) [20].

The σ profile of Caprylic acid and menthol showed two small peaks in the HBD region (σ < -0.01e/Å^2) around -0.013, -0.018 e/Å^2, respectively, the first peak due to a slightly higher peak of menthol and the second peak due to the higher peak of Caprylic acid, related to the hydrogen exposure of the OH group of menthol and the acidic functional group of Caprylic acid.

In the HBA region (σ > 0.01 e/Å^2) of the σ profiles, the peak of Caprylic acid at about 0.012 e/Å^2 was significantly higher than the peak of menthol (about 4.142 vs. 0.741) and then this trend decreased with the increase of σ, and at σ 0.016 e/Å^2, the peak related to menthol was higher.

Conclusion

Molecular dynamics simulations were performed on the Menthol and Caprylic acid-based DES with Caprylic acid (CAP) as the HBD and menthol (MEN) as HBA at the temperature of 298.15 K. The structural analyses, namely RDF and SDF were then conducted to illustrate and confirm the formation of MEN-CAP, and MEN-MEN hydrogen bonds; the results were used to demonstrate the importance of $CAP_{HA}...{}_{O1}MEN$ interactions in the formation of the hydrogen bond network and the results showed that the number of H-bonds formed between MEN and CAP is more than between MEN-MEN. Dynamical properties such as MSD with respect to time were drawn; these were in good agreement with the results of previous analyses. Also, the possible molecular interactions of the mixture of HBA and the HBD (*i.e.* electrostatic, polar, and hydrogen bonding interactions) can be predicted through σ-profiles. These results, therefore, suggested that at the eutectic temperature, the presence of the ring and the OH group of menthol plays an effective role in establishing strong hydrogen bonds. Because possible molecular interactions of HBA and HBD mixture (i.e. electrostatic, polar and hydrogen bond interactions) can also be predicted through σ profile, COSMO-RS analysis also showed that in the structure of MEN and CAP, the part corresponding to the hydroxyl and carboxylic group is more active and the charge density is concentrated in those points, and on the other hand, CAP's donating power and MEN's hydroxyl group's receiving power is greater.

Acknowledgments

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