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IN SILICO POTENTIAL ANALYSIS OF X_6D MODEL OF PEPTIDE SURFACTANT FOR ENHANCED OIL RECOVERY

UJI POTENSI SURFAKTAN PEPTIDA MODEL X_6D SECARA IN SILICO UNTUK ENHANCED OIL RECOVERY

Cut Nanda Sari[1], Usman[1], Rukman Hertadi[2], Tegar Nurwahyu Wijaya[3], Leni Herlina[1], Ken Sawitri Suliandari[1], Syafrizal[1], and **Onie Kristiawan[1]**

[1]"LEMIGAS" R & D Centre for Oil and Gas Technology
Jl. Ciledug Raya, Kav. 109, Cipulir, Kebayoran Lama, P.O. Box 1089/JKT, Jakarta Selatan 12230 INDONESIA
Tromol Pos: 6022/KBYB-Jakarta 12120, Telephone: 62-21-7394422, Faxsimile: 62-21-7246150
E-mail: cutnanda@lemigas.esdm.go.id; E-mail: upararai@lemigas.esdm.go.id; E-mail: kenss@lemigas.esdm.go.id;
E-mail: syafrizal@lemigas.esdm.go.id; E-mail: oniek@lemigas.esdm.go.id;
[2]Biochemistry Research Division, Institut Teknologi Bandung, Jl. Ganesa no. 10 Bandung 40132
[3]Department of Chemistry, Universitas Pertamina, Jalan Teuku Nyak Arief Simprug, Jakarta 12220
Corresponding author: rukman@chem.itb.ac.id

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ABSTRAK

Peptida dan turunannya dapat digunakan dalam Enhanced Oil Recovery (EOR) karena kemampuannya dalam membentuk emulsi dengan molekul hidrofobik. Namun demikian, penelitian peptida untuk aplikasi EOR baik studi secara teoritis maupun komputasi masih sangat terbatas. Tujuan dari penelitian ini adalah untuk menganalisis potensi dari Model X_6D, suatu model peptida surfaktan untuk EOR melalui simulasi dinamika molekuler dalam antarmuka air-minyak. Simulasi dinamika molekuler menggunakan perangkat lunak GROMACS dengan force field Martini dapat menilai kemampuan peptida dalam penataan mandiri (self-assembly) dan emulsifikasi pada skala mikroskopis. Simulasi dinamika molekuler dikombinasikan dengan model coarse grained akan memberikan informasi tentang dinamika molekul peptida dalam antarmuka air-minyak dan perhitungan nilai tegangan antarmuka. Empat rancangan model X_6D: F_6D, L_6D, V_6D, dan I_6D disimulasikan pada antarmuka air-minyak. Nilai tegangan antarmuka dari simulasi menunjukkan tren yaitu $F_6D \cong L_6D > I_6D > V_6D$. Dari hasil terungkap bahwa V_6D memiliki reduksi tegangan antar muka terbesar dan stabilitas hingga 90°C dengan salinitas sekurang-kurangnya 1M NaCl.

Kata Kunci: *peptida surfaktan, analisis potensi, Model X_6D, enhanced oil recovery*

ABSTRACT

Peptides and their derivatives can be applied in enhanced oil recovery (EOR) due to their ability to form an emulsion with hydrophobic molecules. However, peptide research for EOR application, either theoretical or computational studies, is still limited. The purpose of this research is to analyse the potency of the X_6D model of surfactant peptide for EOR by molecular dynamics simulations in oil-water interface. Molecular dynamics simulation using GROMACS Software with Martini force field can assess a peptide's ability for self-assembly and emulsification on a microscopic scale. Molecular dynamics simulations combined with coarse grained models will give information about the dynamics of peptide molecules in oil-water interface and the calculation of interfacial tension value. Four designs of X_6D model: F_6D, L_6D, V_6D, and I_6D are simulated on the oil-water interface. The value of interfacial tension from simulation show the trend of $F_6D \cong L_6D > I_6D > V_6D$. The results indicate that V_6D has the greatest reduction in interfacial tension and has the stability until 90°C with the salinity of at least 1M NaCl.

Keywords: peptide surfactant, potential analysis, X_6D model, enhanced oil recovery

I. INTRODUCTION

Peptides are polymers made of amino acids linked by amide bond. Peptides are naturally occurring in nature, and mostly incorporate with other molecules such as lipids and carbohydrates, or form a polypeptide to become protein. There are at least 20 peptide-forming amino acids thereby providing flexibility in the function and characteristics of the peptides formed (Youseff et al. 2013). These properties make peptides an attractive material to be studied and applied in various fields such as constituent nanomaterial, surfactant, food additives, and *microbial enhanced oil recovery (MEOR)* (Dong et al. 2008; Hamley et al. 2014; Vauthey et al. 2002; Dexter & Middelberg, 2008; Simpson et al. 2011; Adjonu et al. 2014).

Surfactant peptides are peptides comprising hydrophilic amino acid residues (polar or charged amino acids) in one side and hydrophobic amino acid residues in the other side (Dexter & Middelberg, 2008). Furthermore, surfactant peptides are able to bind with a long chain alkyl group as a "tail" and hydrophilic amino acids as the "head" of the surfactant. Several peptides have been designed and investigated as surfactant (Perez et al. 2014). Therefore, information about the properties, structure and orientation of the surfactant molecules and peptide interactions within oil-water phase in the molecular level is required in the process of designing new surfactant peptides.

Molecular dynamics simulations are used to simulate the movement of a peptide molecule in the oil-water phase or interface. Combined with coarse grained models, molecular dynamics simulation can be run in economic computing devices with acceptable result. Several studies have been conducted to determine the oil-water interfacial tension on conventional surfactant molecular dynamics simulations (Xu, 2013 & Herdes et al. 2015).

The main objective of this research is to analyse the potency of X_6D model of surfactant peptide for EOR by molecular dynamics simulations in oil-water interface. The results from this simulation will provide information for advancing experiments in peptide designs.

II. METHODOLOGY

Four designs of X_6D model: F_6D, L_6D, V_6D, and I_6D are simulated using coarse grained models. Interfacial tension values are predicted by the presence or absence of peptide, in addition to predicted concentrations of different peptides. The oil phase isrepresented by octadecane molecules.

A. Structure Construction and Coarse Grained Model

At three-dimensional structure of surfactant peptides is constructed using a Molefacture program, which is available in the software VMD (Humphry *et al*., 1996). The obtained structure was in the form of a pdb file and was converted into a coarse-grained models using martinize.py program (available from the website *cgmartini.nl*). The constructed models of 4 surfactant peptides are V_6D, F_6D, I_6D, and L_6D with the amino acid composition as listed in Table 1.

Three-dimensional structure of the coarse-grained molecular models octadecane (C18) were constructed manually using the Molefacture program by length and angle parameters in octadecane molecular bond in the beam martini_v2.0_solvents. itp (Martini force field) (Marrink *et al*., 2017). The water molecules model was obtained from *cgmartini. nl* website. simulation box of 6 x 6 x 24 nm with the water phase in the centre of 12 nm (approx.) on the axis and the oil phase (octadecane) at 6 nm

Table 1
Composition and hydropathy index of amino acids forming a model surfactant peptide

Peptide Surfactant Model	Amino Acid Composition (N terminal → C terminal)	Hydropathy Index[12]
V_6D	val-val-val-val-val-val-asp	val 4.2; asp -3.5
F_6D	phe-phe-phe-phe-phe-phe-asp	phe 2.8; asp -3.5
I_6D	ile-ile-ile-ile-ile-ile-asp	iso 4.5; asp -3.5
L_6D	leu-leu-leu-leu-leu-leu-asp	leu 3.8; asp -3.5

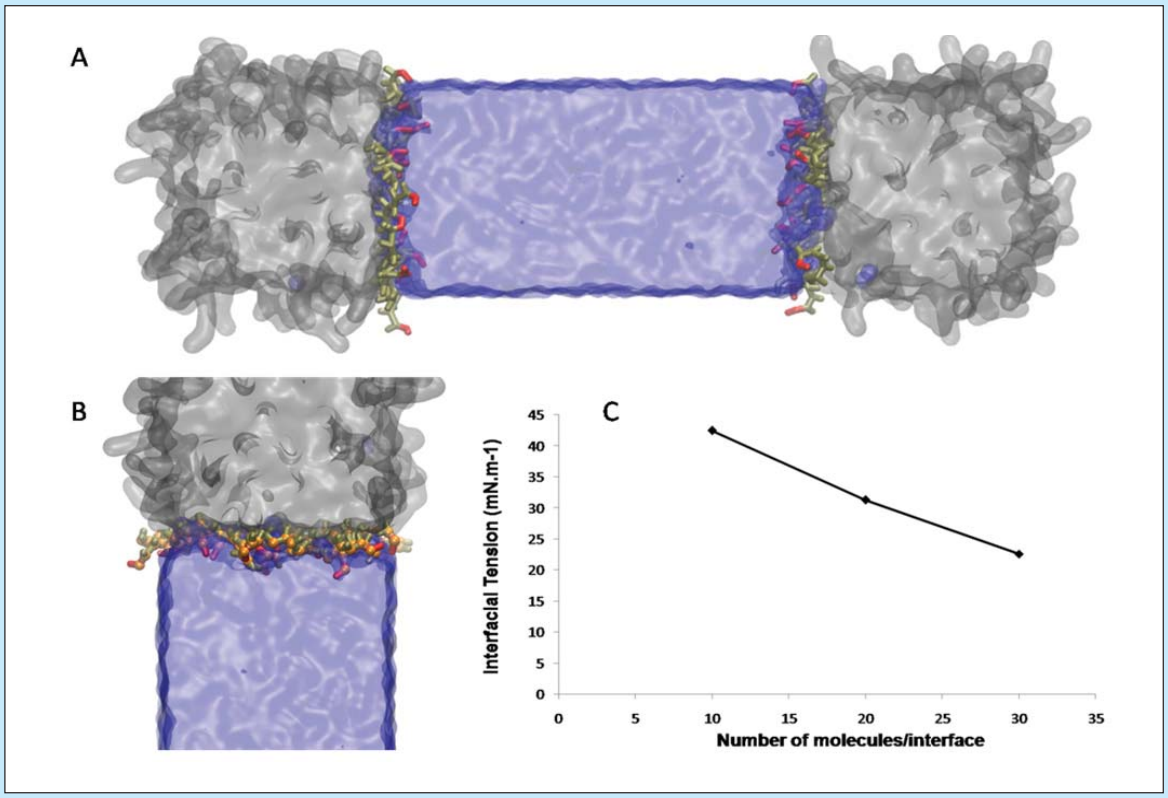

Figure 1
(A). The simulation results in 10 ns. Blue indicates water phase, gray indicates oil phase, red indicates aspartate residue, and dark brown indicate valine residue. (B). Peptide molecular orientation at the oil-water interface. Goldenrod indicates peptide backbone. (C). Interfacial tension as a function of the number of peptide molecules per interface.

at the ends of the box along the z axis. The peptide was placed in the oil phase near the interface at the commencement of the simulation. Thus there are two oil-water interface in one simulation box which contains the same amount of peptide on each interface. Neutralizing ions were added in the water phase.

B. Simulation Details

The simulations were run using Gromacs software version 5.0.4 which can be downloaded for free from *www.gromacs.org* (Berendsen et al. 1995; Lindahl et al. 2001; Van Der Spoel 2005; Hess et al. 2008). Simulations were run with Martini force field using version 2.2 (Marrink et al. 2007 & Monticelli, 2008). Surface tension value is obtained by running simulations on ensemble NVT for 10 ns at 298°K. Surface tension value is extracted directly from GMX energy programs (available in Gromacs) using simulated data from 2 to 10 ns. Simulated temperature is maintained at 298 K using v-rescale algorithm. By using coarse grained structure, the interval of integration time can be increased up to 20 fs. Electrostatic and van del Waals interaction is calculated using the potential shift with cut-off at 1.2 nm and potential switch at 0 and 0.9 nm for each electrostatic and van der Waals interaction. Electrostatic calculation parameters have been modified to Martini force field.

The advance simulations run were based on the number of peptides in order to know the relationship between peptide concentration with interfacial tension decrease. Two additional simulations run with peptide amounts of 10 and 30 molecules per surface area (3.6 and 1.2 nm^2 per molecule of peptide, respectively).

For surfactant stability test, the simulation conducted at temperature of 25, 50, 75, and 90°C and at salinity of 0.25, 0.5, 0.75, and 1 M NaCl, to determine the effect of temperature and salinity on the interfacial tension value of the oil-water interface on the addition of the best peptide design.

III. RESULTS AND DISCUSSION

A. The Orientation of Surfactant Peptide Molecules in the Oil-Water Interface

The results of simulation showed that peptides assembled at the interface of water and oil to the position of charged residues (aspartate) facing the water while nonpolar residues facing the oil (Figure 1 AB for peptide V_6D).

When compared with conventional surfactants, surfactant peptides have unique characteristics due to the chemical structure of the peptide molecule. In conventional surfactants, surfactant molecules have a hydrophobic part of the head and a hydrophilic part of the tail (Xu, J. et al. 2013). This characteristic causing the entire tail is in oil phase while the entire head is in the water phase, consequently surfactant molecules will be oriented perpendicular to the oil-water interface. The surfactant peptide consists of three parts: the backbone, hydrophilic side chain residues, and hydrophobic side chain residues. The backbone is in the middle between hydrophilic side chain residues and hydrophobic side chain residues. The backbone has more hydrophilic than hydrophobic side chain residues. This characteristic makes the surfactant peptide oriented parallel to the oil-water interface. This is confirmed by the simulation that the backbone tends to be in the water phase together with hydrophilic side chain residues, while hydrophobic side chain residues tend to be in the oil phase (Figure 1B). The differences in the molecular orientation of surfactant peptides will create different physical properties from conventional surfactants. The ability of the peptide to form an emulsion is greatly influenced by hydropathy residues which form the "tail" of surfactant. However, the experimental data such as critical concentration of micelle formation,

Table 2
Interfacial tension simulation results

Model/system	Interfacial Tension ($mN.m^{-1}$)
Oil-water	49.303
Oil-water-F_6D	37.479
Oil-water -L_6D	37.146
Oil-water-V_6D	31.287
Oil-water-I_6D	34.845

*The amount of peptide per one interface is 20 molecules (1.8 nm^2 area per molecule).

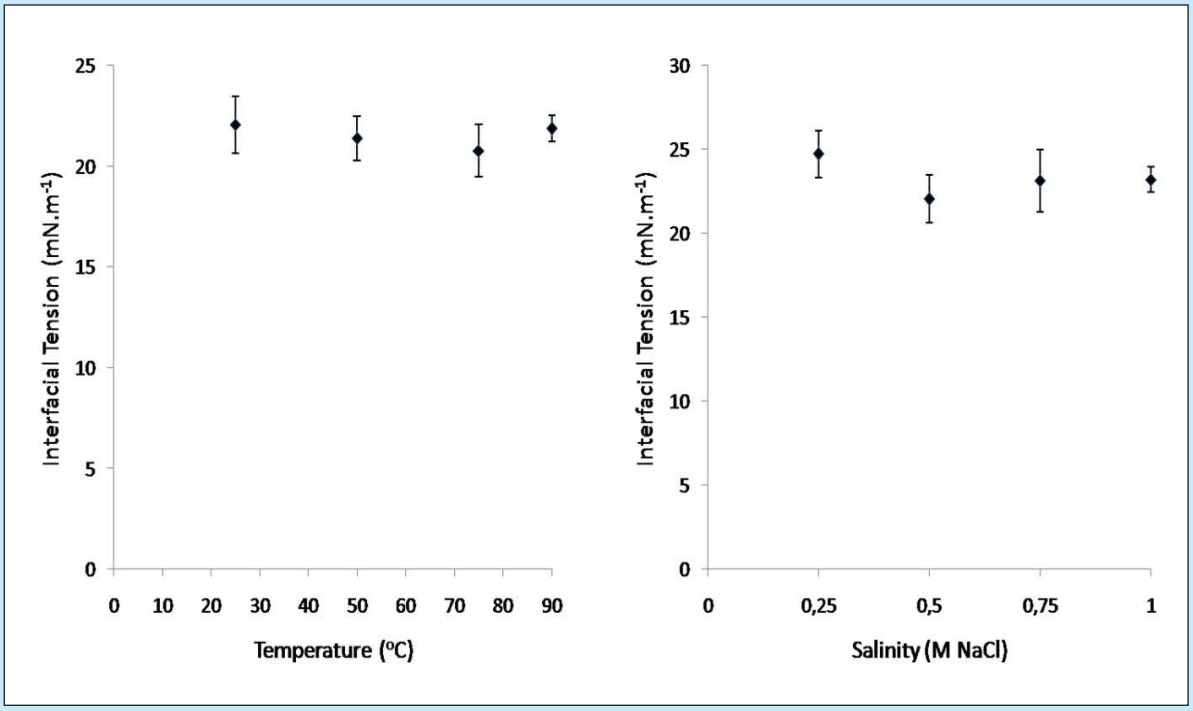

Figure 2
Interfacial tension values based on temperature (A) and salinity (B). Vertical lines indicate standard error of molecular dynamics simulations.

surface area per molecule. are required to find out the differences in the physical properties.

B. Interfacial Tension Calculation Using Simulation

The value of the oil-water interfacial tension by molecular dynamic simulation is presented in Table 2. The simulation results show interfacial tension decreases along with peptide addition. V_6D have the lowest interfacial tension value among the 4 peptide designs. The value of interfacial tension follows the trend of $F_6D \cong L_6D > I_6D > V_6D$.

The interfacial tension value from all peptide models show inversely with the hydropathy index. The hydropathy index is proportional to the hydrophobic residue. The more hydrophobic a peptide, the higher its hydropathy index. With the equal charged of amino acid, i.e asparthate, the effectiveness of the peptide as a surfactant depends on the hydropathy index of hydrophobic residues which interact with oil-phase. Although the hydropathy index of valine is slightly lower than isoleucine (4.2 and 4.5 respectively) there is a great difference between their interfacial tension value. We suspect other factors that play a role when the hydropathy index between two residues has no significant difference. The factors can be derived from the structure of the side chains of amino acids or comes from how Martini force field remodelling of these residues. Additional data from experiments or simulations are needed to confirm these factors (Marrink et al. 2007).

The simulation using V_6D peptide showed a linear correlation between the number of peptide molecules and the interfacial tension value (Figure 1C). The higher the number of molecules, the lower its interfacial tension. When concentration is greater than the CMC, the addition of the surfactant molecule concentration will not decrease the value of interfacial tension. It can be concluded that the concentration of peptides in this simulation is lower than the CMC value. In other words, the potency of peptide is not optimally exploited yet, therefore, there are possibilities for surfactant peptides to be applied as a surfactant.

Although the interface tension value can be obtained from molecular dynamics simulations using Martini coarse-grained models, the interface tension value is not in accordance with experimental results. For example, surface tension of pure water from theexperiment test show the value of 72 $mN.m^{-1}$ while the results of molecular dynamics simulations was in the range of 32 $mN.m^{-1}$. It should be understood that the calculation of the value of this study of interfacial tension can only be used as qualitative guidance as to how a peptide can reduce the surface tension. As a result, the interfacial tension value from the simulation in this study should not be compared quantitatively with experimental results. The advance otimization of force field optimization is needed to correct the problem.

C. Surfactant stability Based on Temperature and Salinity

The stability of surfactant peptide V_6D wes tested in temperature and salt concentration variation. Figure 2 shows that there is no significant change on interface tension values when the temperature increase up to 90°C. It is indicated by the values were in the range of standard error. The simulation results also show that the tension is stable at a salinity of 0.25 to 1 M NaCl. These results suggest that the peptide V_6D can be apply in the field with high temperature or high salinity levels.

The simulation results can be used as a reference in peptides designing for EOR or emulsification purposes and as comparation of the characteristics between peptide surfactants and other surfactants peptides. The ability of the peptide to form an emulsion greatly influenced by hydropathy residues which form the “tail” of surfactant.

IV. CONCLUSION

Molecular dynamics simulation can be used to predict the qualitative value of interfacial tension of oil-water system in the presence of peptide surfactants. Moreover it can be used to observe the process of structuring self peptide molecules into regular secondary structure.V_6D peptide has a potency for EOR application. However, advanced laboratory experiments laboratorium is required before the application of V_6D peptide as a surfactant.

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