

Full Length Research Paper

Quantum mechanic studies on dipalmitoylphosphatidylcholine and dimyristoylphosphatidylcholine as nanoscales of membrane

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An understanding of static properties of membrane is an essential prelude to the study of movement of molecules within the membrane. In this investigation two molecules have been theoretically investigated through the quantum mechanical calculations. According to the obtained results of the structural optimization of the isolated DPPC (dipalmitoylphosphatidylcholine) and DMPC (dimyristoylphosphatidylcholine) in the gas phase, at the Hartree-Fock level utilize sto-3g,3-21G, 6-31G and 6-31G* basis sets. the most important dihedral angle of these molecules (DPPC and DMPC) have chosen and the energy, dipole moment, and atomic charges of 14 important atoms have scanned within 180 degrees rotation and sites that have most changes have determined and any rotated molecule separately has placed in the 19 solvents (The method is HF/6-31g* model) and then dielectric effect of surrounding has analyzed. The solvent effect on the stability of DPPC and DMPC molecule, dipole moment, and atomic charge of some atoms of those molecules have been discussed by using onsager model.

Key words: Dipalmitoylphosphatidylcholine (DPPC), dimyristoylphosphatidylcholine (DMPC), quantum mechanics (QM), abinitio, solvent effect.

INTRODUCTION

DPPC and DMPC are taken as phospholipids with an equal polar head and with difference in the length of hydrocarbon chains. One of the great challenges in biophysics that understand the basic principles governs lipid bilayer mixtures. Lipid bilayers, or membranes, govern and mediate various biologically relevant processes on the cellular level (Patra et al., 2003; Monajjemi et al., 2007).

Membranes are semi permeable, highly selective barriers containing ion channels and pumps to modulate and maintain balance as required. Important energy conversion and storage processes take place at the membrane level. Consequently, a fundamental

understanding of bilayers and membrane proteins from the atomic point of view is of great biochemical, biophysical and medical interest (Moore et al., 2001; Haeri et al., 2007).

Significant progress has been made toward understanding some of the key characteristics of both lipids and membrane proteins which determine the favorable energetic of bilayer environment (Petrache et al., 2002).

Many physical and biochemical properties are now commonly investigated by atomistic molecular dynamics (MD) simulation and quantum mechanics (QM) (Monajjemi et al., 2008; Jiang et al., 2004).

Membranes are asymmetric structures. The choline-containing phospholipids are located mainly in the outer molecular layer (Murray et al., 2000). This asymmetric distribution is maintained by an ATP-dependent protein

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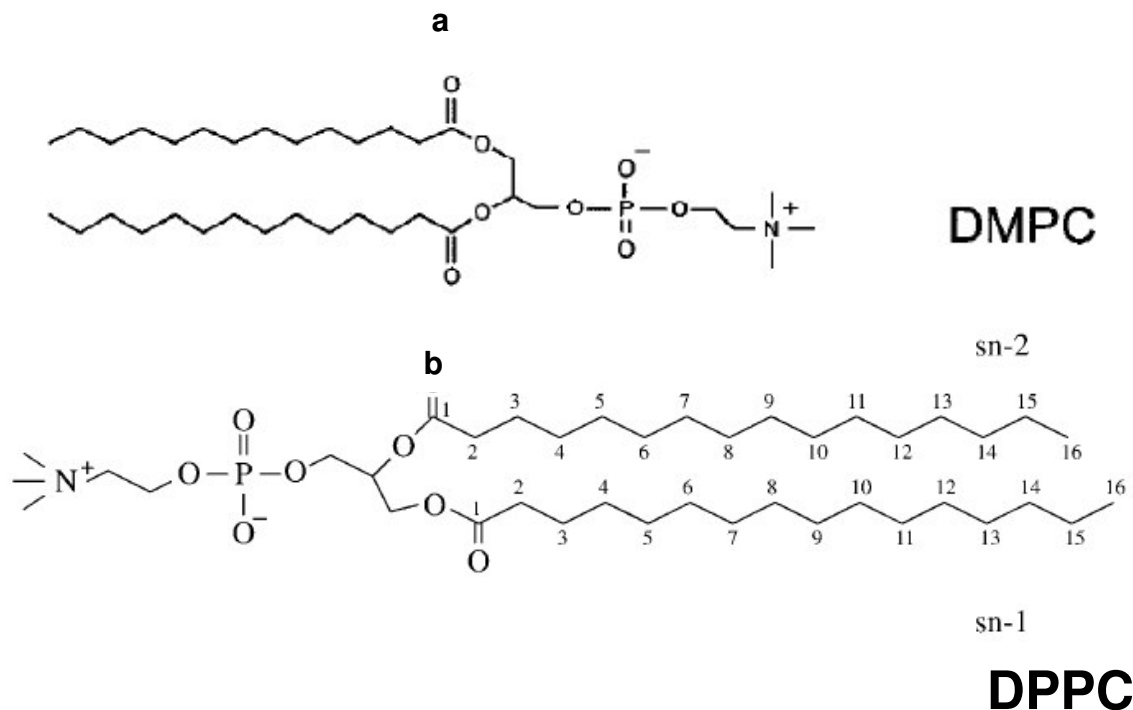


Figure 1. DPPC and DMPC molecule.

which specifically translocates phosphatidylethanolamine to the inside of the plasma membrane (Zachowski et al., 1986).

All major lipids in membranes contain both hydrophobic and hydrophilic regions and are therefore termed amphipathic. Dipalmitoylphosphatidylcholine (DPPC) and dimyristoylphosphatidylcholine (DMPC) are taken as phospholipids with an equal polar heads and with the difference in the length of hydrocarbon chains (Murray et al., 2000; Kiselev et al., 2000). These two molecules have saturated fatty acid tail groups (Yun, 2003).

On a molecular level it has been of interest to explore to what extent PC head groups differ with respect to molecular conformation, lateral interactions and dipole arrangements and how these features affect the properties and topology of the membrane surface (Landin and Pascher, 1997; Robinson et al., 1994). DPPC and DMPC are important phospholipids in cell bilayer, then investigation of interaction between peptides and bilayer of these molecules is very important (Haberman and Jentsch, 1967). DPPC has gel to liquid crystalline transition temperature (T_m) of 41.5 degree of centigrade and at a physiological temperature of 37 degree of centigrade; it is in an ordered gel state (Gulik et al., 1994).

These two molecules are zwitterionic having a negative charge on the phosphate group and a positive charge on the amine. The hydrocarbon chain of DPPC and DMPC have 16 and 14 carbons long, respectively (Figure 1), then the solvent effects on these molecules are important

(Moore et al., 2001; Kova et al., 2005).

In this work we have use of the *ab initio* calculations to determine minimum energy conformations of the dimyristoyl phosphatidylcholine and Dipalmitoylphosphatidylcholine and have performed calculations according to the continuum solvating model by Onsager (Monajjemi et al., 2007a; Monajjemi et al., 2007b; Monajjemi et al., 2006; Shabani et al., 2003; Rajaeian et al., 2003).

COMPUTATIONAL METHODS

All calculations have been done by *ab initio* at the Hartree-Fock (HF) level of theory Gaussian 98 package (22). Four basis sets have been used inclusive the sto-3G, 3-21G, 6-31G and 6-31G*. The geometry of DPPC, DMPC have been optimized at the RHF/6-31G*, 6-31G, 3-21G and STO-3G levels of the theory in the gas phase.

The most important dihedral angle of these molecules (DPPC and DMPC) is chosen of head molecule outweigh tail molecule and the energy, dipole moment, and atomic charges of 15 important atoms have scanned within 180 degrees rotation. In this manner after the optimization of total molecules, important dihedral angle of these molecules has rotated 15 degrees at every time.

The effects of the solvent polarization are described in terms of proper QM operators to be added to the Hamiltonian of the isolated system. Then, the solvation calculations have performed using Onsager method at HF/6-31G*. For Onsager model, it requires values of volume (a_0) of the molecule and the dielectric (ϵ) constant of solvent. The volume of DPPC and DMPC molecules was obtained using the "volume" key word. The basis set is 6-31G* and 13 a_0 for DPPC is 7.77, 7.26, 7.49, 7.05, 7.38, 7.59, 7.77, 7.27,

Table 1. Conformational energy of DPPC and DMPC obtained by geometry optimization for different basis set.

Basis set	E/kcal.mol	E/kcal.mol
	DPPC	DMPC
Sto-3G	-1583811.262	-148406.112
3-21G	-1594584.634	-149458.505
6-31G	-1602682.003	-1505418.2
6-31G*	-1603386.341	-1505422.1

7.59, 6.93, 7.31, 7.60, 6.95 and 13 a_0 for DMPC is 7.29, 7.25, 7.49, 7.32, 7.42, 7.26, 7.17, 7.34, 7.37, 7.24, 6.96, 6.84, 7.42).

The Onsager-SCRF has permitted one to directly exploit almost all of the computational facilities of the Gaussian 98 program package. For this reason and for its very limited computational cost, it is still in use by people not requiring an accurate description of solvation effects but just a guess or a qualitative correction to the values obtained for the isolated molecule. Users must be aware of the limitations of the approach, of the unphysical deformation of the solute charge distribution it may induce and of other shortcomings specific of the approach, such as the lack of solvation for solutes with zero permanent dipole.

In the Onsager method, the solute molecule is placed in a spherical cavity of radius a_0 surrounded by a continuum with constant dielectric properties (Landin and Pascher, 1997). A dipole in the molecule will induce a dipole in the medium, and the electric field applied by the solvent dipole will in turn interact with the molecular dipole leading to net stabilization. The molecular geometrics have obtained via HF/6-31G* level optimization in the gas phase and have rotated and then any one separately have been placed in the 19 solvents. The solvents are water ($\epsilon = 78.39$), dimethylsulfoxide ($\epsilon = 46.7$), nitromethane ($\epsilon = 38.2$), acetonitrile ($\epsilon = 36.64$), methanol ($\epsilon = 32.63$), ethanol ($\epsilon = 24.55$), acetone ($\epsilon = 20.7$), dichloroethane ($\epsilon = 10.36$), dichloromethane ($\epsilon = 8.93$), tetrahydrofuran ($\epsilon = 7.58$), aniline ($\epsilon = 6.89$), chlorobenzene ($\epsilon = 5.621$), chloroform ($\epsilon = 4.9$), Ether diethylether ($\epsilon = 4.335$), toluene ($\epsilon = 2.379$), benzene ($\epsilon = 2.247$), carbontetrachloride ($\epsilon = 2.228$), cyclohexane ($\epsilon = 2.023$) and heptane ($\epsilon = 1.92$).

The total energy of solute and solvent, which depends on the dielectric constant and also dipole moment of solute, induces a dipole moment of opposite direction in the surrounding medium (Monajjemi et al., 2007a; Monajjemi et al., 2007b; Monajjemi et al., 2006; Shabani et al., 2003; Rajaeian et al., 2003).

RESULTS AND DISCUSSION

Dipalmitoylphosphatidylcholine (DPPC) and dimyristoylphosphatidylcholine (DMPC) molecules have chosen as starting structures for gas phase (Figure 1). The DPPC and DMPC zwitterionic are found to be unstable in the gas phase when have optimized at HF/3-21G, 6-31G and 6-31G* level (23). The obtained result from optimization and stabilization parameters are shown in Table 1.

The minimum energy have been obtained by 6-31G* basis set. Therefore we selected basis set 6-31G* for other calculation in this work. The most important dihedral angle of these molecules (DPPC and DMPC) is chosen by optimization of total molecules (Figure 2a, b) and then these molecules have been rotated every time 15°.

Alteration of dipole moments and energies of these rotations have been shown in Figure 3a, b. A communicating is between dipole moment with energy and rotation angle. First, angle of most important dihedral is 60° that every time increase 15 degree (Table 2). The minimized energy about DMPC and DPPC is in the 60° and other minimized energy is in the 150°. In Figure 3 is observed a minimum energy that coordinates with maximum dipole moment. Comfortably, it can correspond to relation between dipole moment and energy with rotation angle. Consequently in maximum dipole moment, DMPC and DPPC molecule are the permanent state. Alteration of angle and atomic charge of these rotations are shown in Figure 4a, b.

The maximum charge phosphorus (p57 in DMPC, p63 in DPPC) is in 105 degree that coordinates with angle hybridation. In DPPC P63 decreases the charge in 160 degree that synchronous O67 has a increased charge. It has been observed increased partial charge in minimum state for O48 and a severe deduction in O66 that causes energy evacuation that similar electroscope sheet charge is transferred to tail.

The same result is observed for DMPC. Most chemical reactions and biological process take place in solutions. The use of the SCRF model in quantum-chemical theory requires that the shape and volume of the solute molecule must be defined uniquely for any set of compounds.

A number of approaches to calculate these characteristics are known, but no non-empirical methods for their estimation have been developed. However, from the result of model calculation it may be concluded that the simple model assuming a spherical or an ellipsoidal shape of the cavity for the solute molecule is probably satisfactory for comparatively small and rigid molecules.

We present a quantum-chemical analysis of the solvent effect on stability of molecule, dipole moment and by corresponding to atomic charge of some selected atoms of DPPC and DMPC molecule. The molecular geometrics are obtained via HF/6-31G* level optimization in the gas phase and then important dihedral angle of these molecules have rotated every time 15 degrees and every time, the volume of DPPC and DMPC molecules have obtained using the "volume" keyword. Any one of rotated molecule separately placed in the 19 solvents (Key word, scrf = dipole).

Regular alterations were observed concerning energy

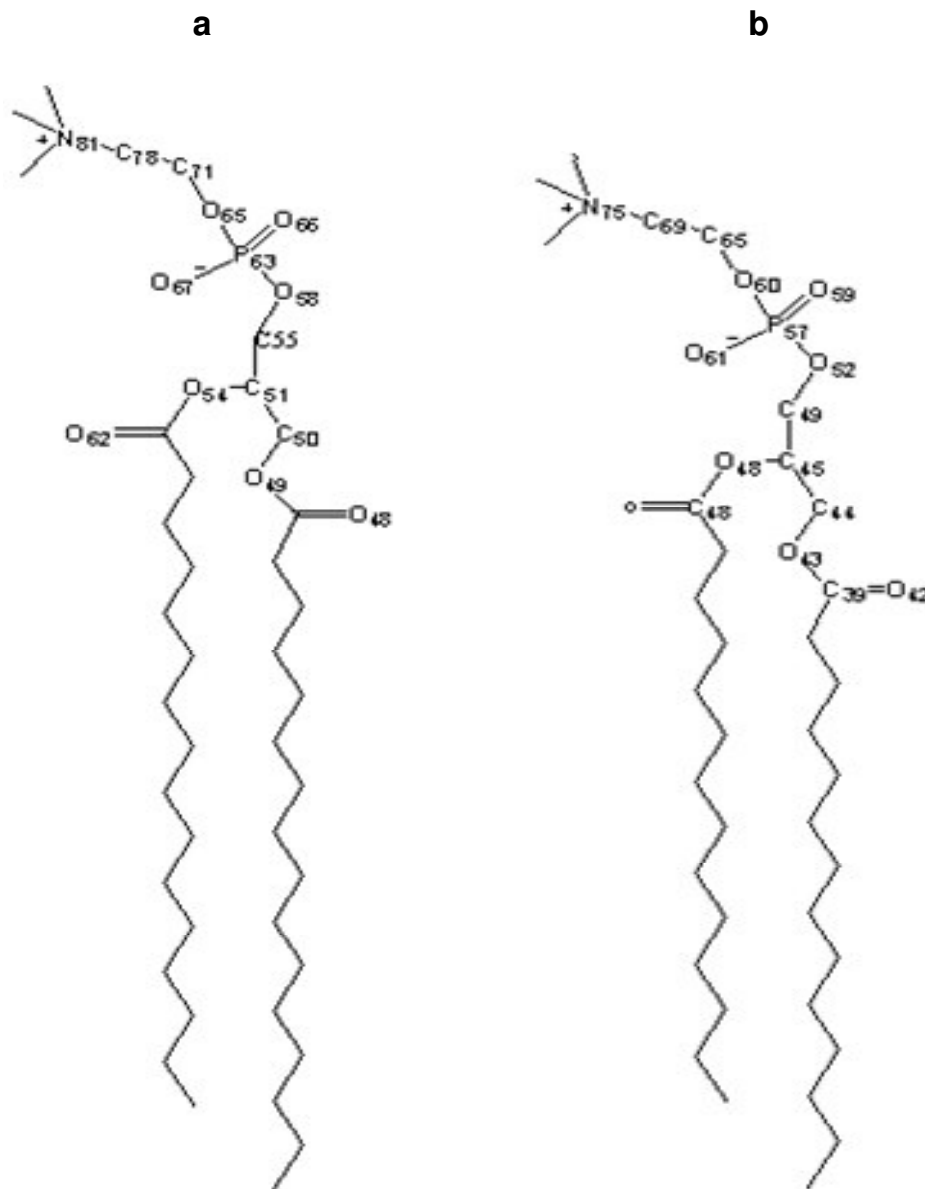


Figure 2(a). Atom numbering of DPPC **(b).** Atom numbering of DMPC.

versus dielectric constant. With increasing of dielectric constant of solvents, stability of 13 AO values of DPPC and DMPC increase (Figure 5a, b).

The computed solvent-dependent acceptor and donor charge distributions for some atoms in each medium are shown on Figure 6a, b.

As it was expected, where the charges of the many atoms (C45, C49, C44, O42, O48, O59 of DMPC and C51, C55, C50, O48, O54, O66 of DPPC) are increasing when the dielectric constant is increasing. But the charges of many atoms (P57, C65, N75, O56, O43, O52, O61, O60 of DMPC and P63, C71, N81, O62, O49, O57, O67, O65 of DPPC) are decreasing when the dielectric constant (D) is increasing.

Conclusions

We compare DMPC and DPPC molecule in membrane to electroscope that using external charges on the ball of electroscope can regulate handicap distance of angle between two sheets of electroscope. The role of this ball is the same role of phosphorus in the membrane molecules and the hydrocarbons chains have the same role of electroscope sheet. Hydrophobic and hydrophilic forces of charges accruing on metal ions at the time that effect on membrane create one charge induction in the phosphorus atom. This charge induction effect on the hydrocarbons chains and cause particular dynamic movement of phospholipids. This dynamic movement

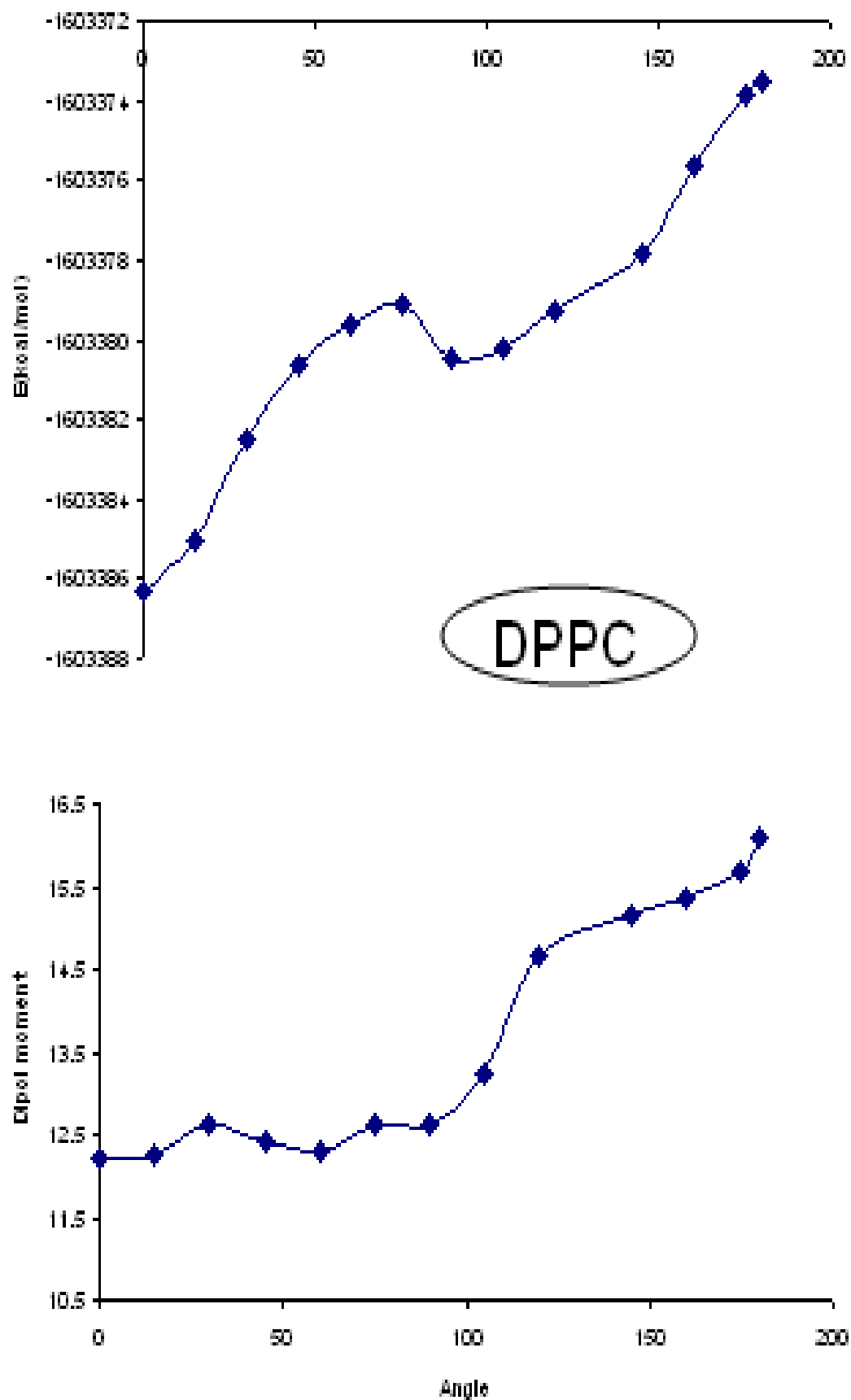


Figure 3a. Energy and Dipole moment versus Angle for DPPC

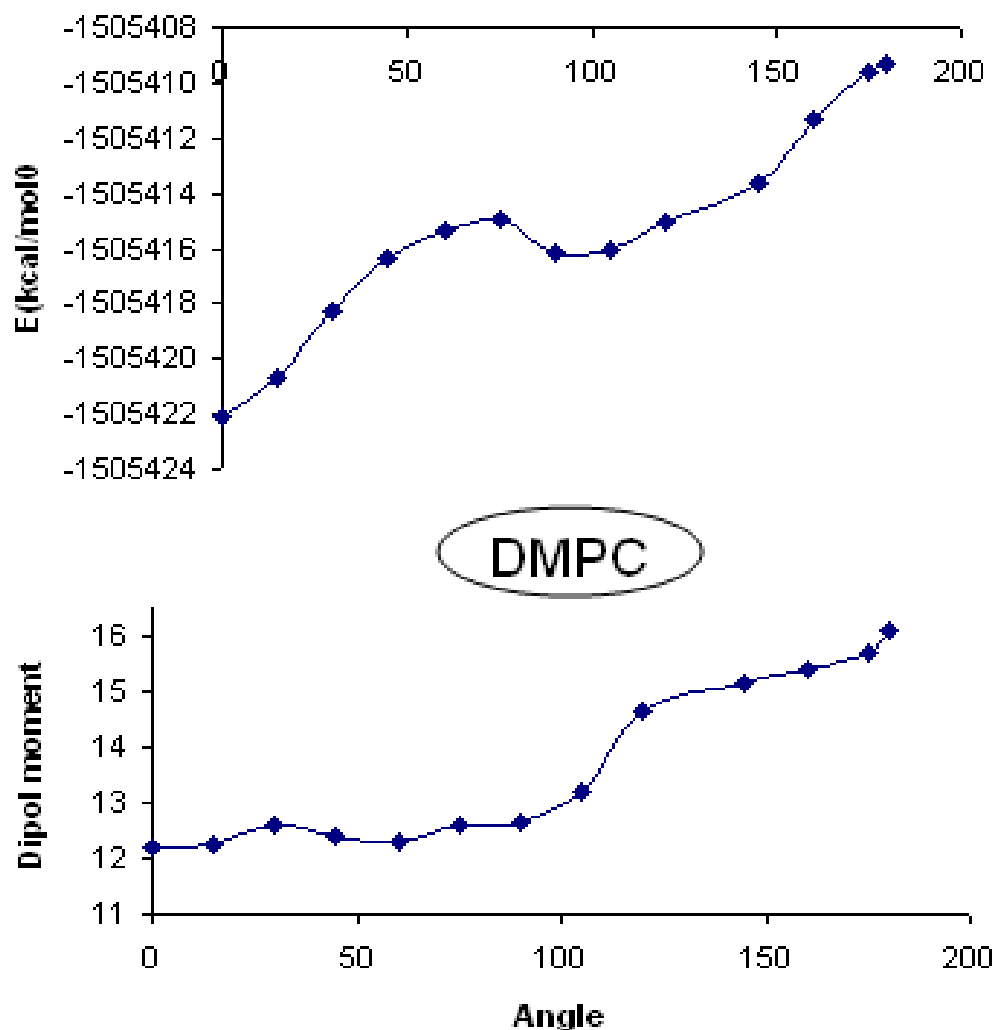


Figure 3b. Energy and Dipole moment versus angle for DPPC and DMPC.

Table 2. Different rotation in most dihedral angle of DPPC and DMPC.

	Angle	Rot
DPPC	60	0
	75	15
	90	30
	105	45
	120	60
	135	75
	150	90
	165	105
	179.9264	120
	-165.0748	145
	-150.0753	160
	-135.0739	175
	-120.076	180

Table 2. Continued.

DMPC	60	0
	75	15
	90	30
	105	45
	120	60
	135	75
	150	90
	165	105
	179.9345	120
	-165.0669	145
	-150.0664	160
	-135.0664	175
	-120.0655	180

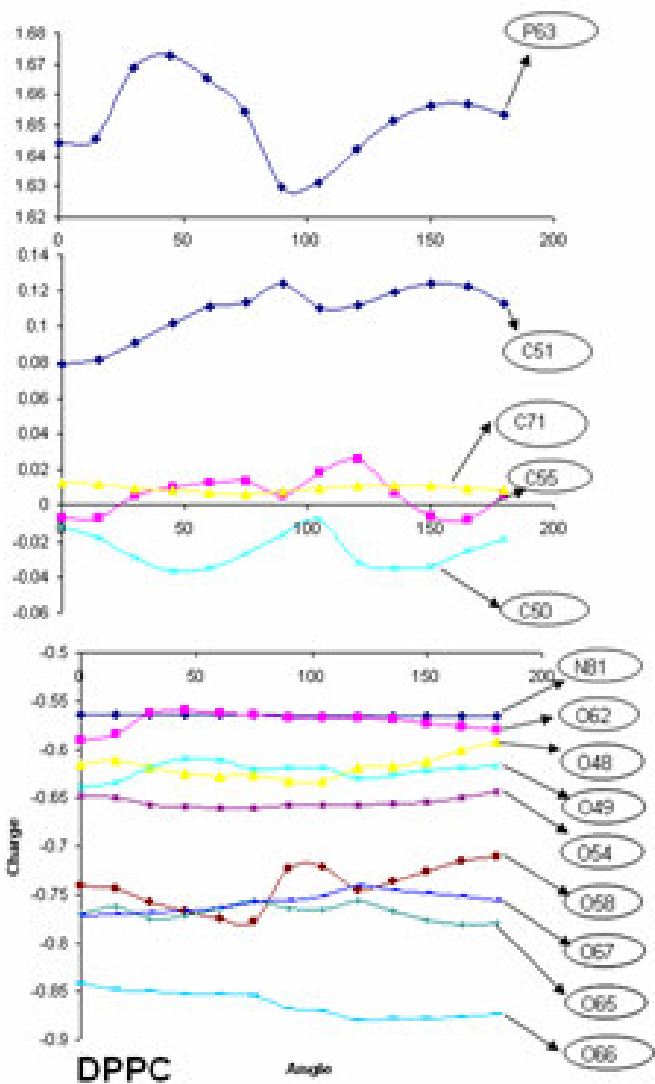


Figure 4a. Atomic charge versus Angle for DPPC

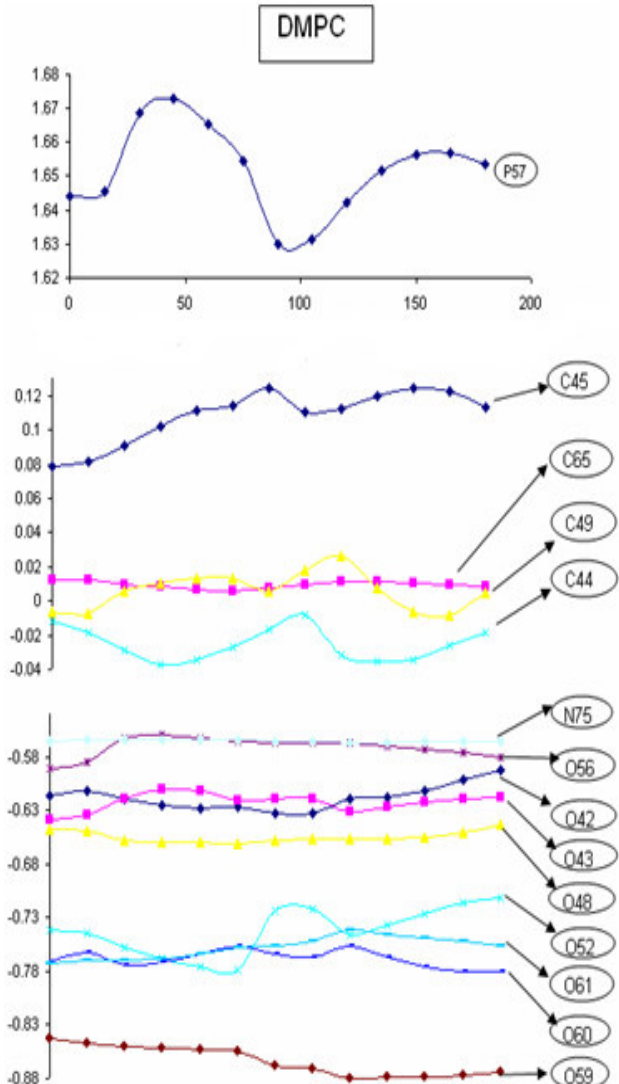


Figure 4b. Atomic charge versus Angle for DMPC.

(a)

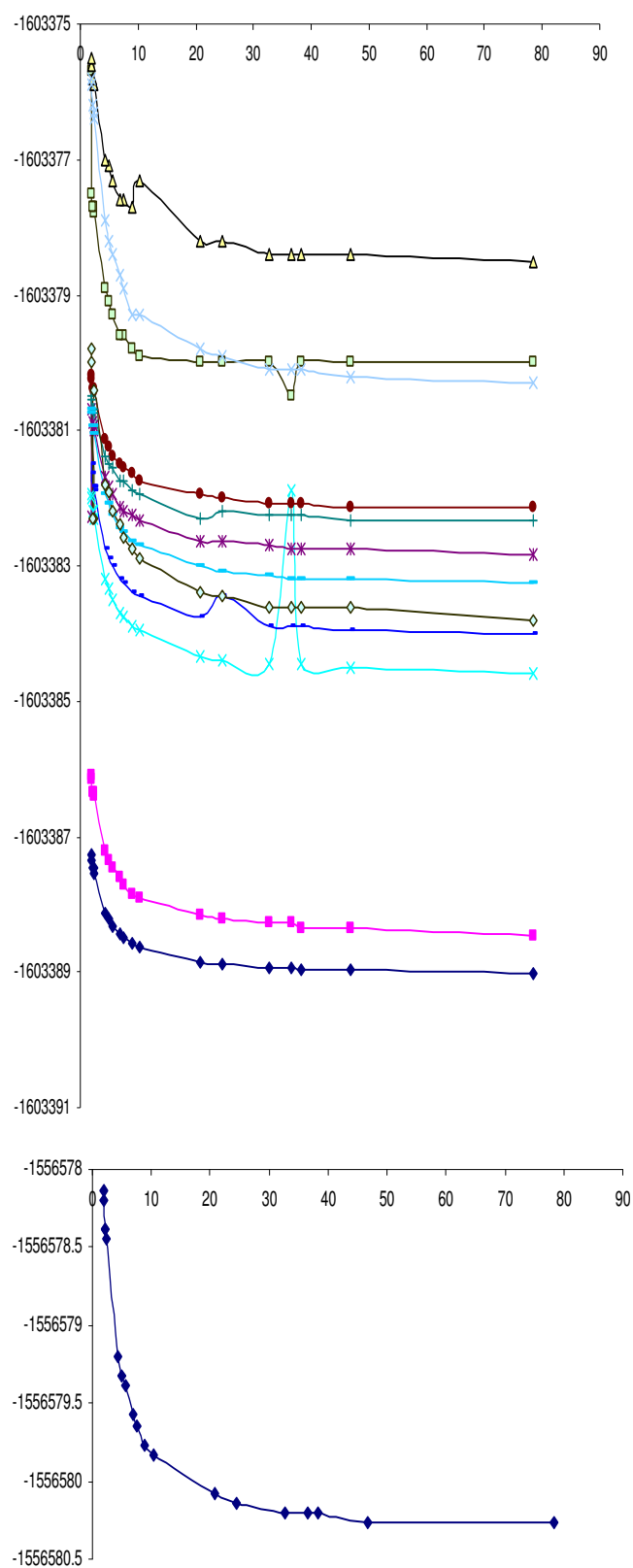


Figure 5a. Energy (kcal/mol) versus Dielectric constant for 13 a0 values DPPC

(b)

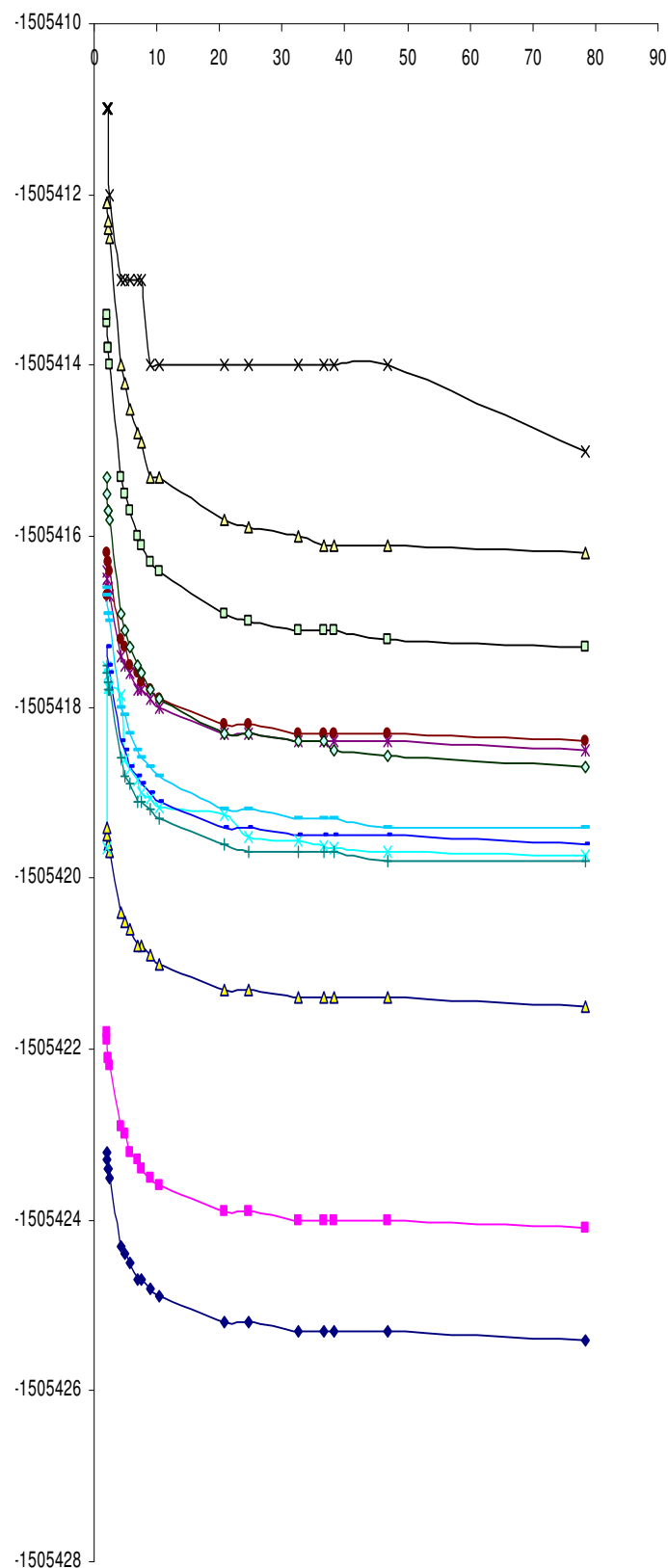


Figure 5b. Energy (kcal/mol) versus Dielectric constant for 13 a0 values DMPC

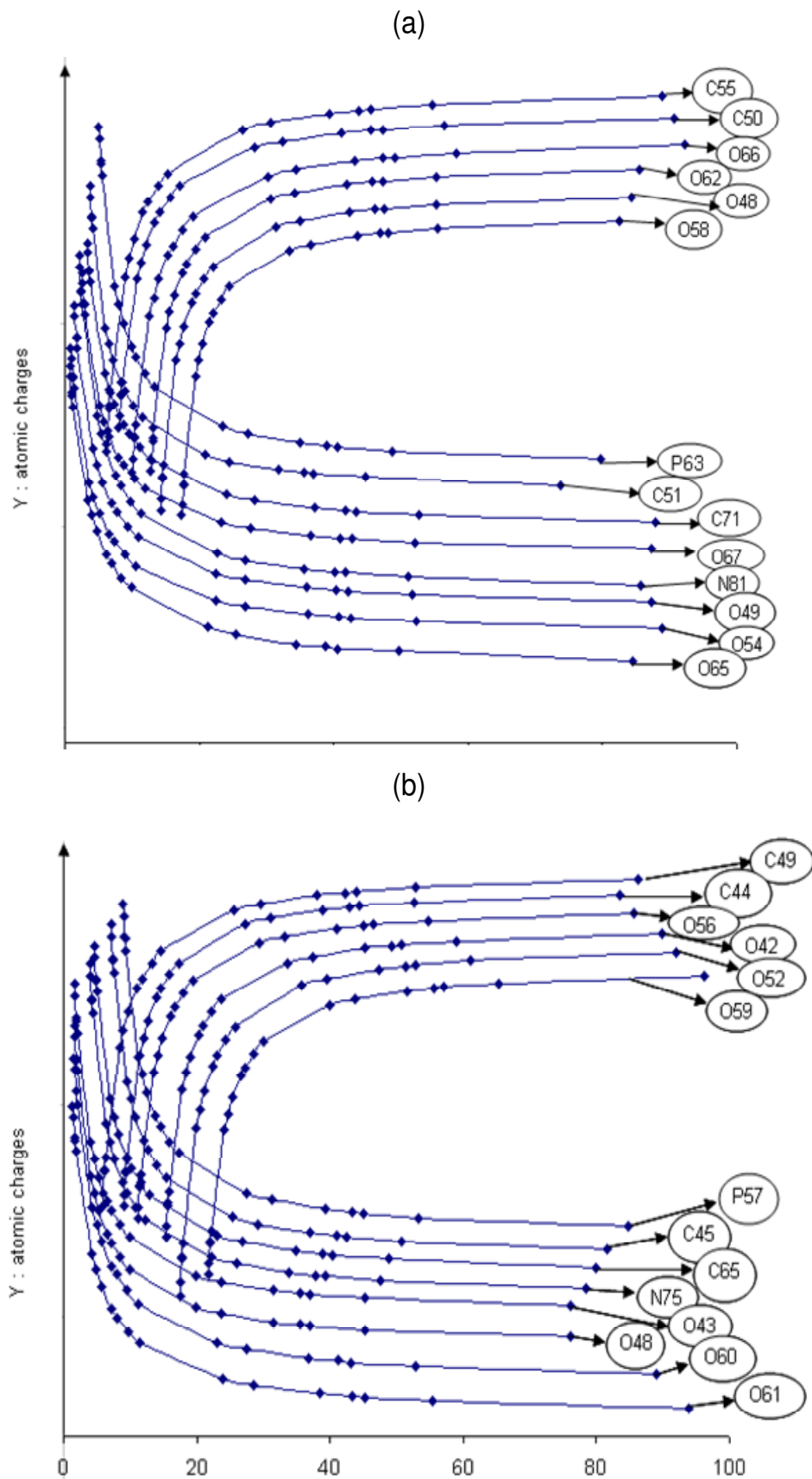


Figure 6. Dielectric constant versus Atomic charge of (a) DPPC and (b) DMPC

cause to enter and exit material to or of cytoplasm membrane. Our exertion in this investigation is determine agents such as atom partially charges on dipole moment and dielectric constant in angle between chain-phosphorus-chain that results this notation.

1-A communicating is between dipole moment with energy and rotation angle

2-The most P charge was in 105 degree that coordinates with angle hybridation

3-Synchronus to induction charges in phosphorus is observed addition charge in oxygen

4-Coordination between O62, O49, C50, and N81 in DPPC Totally can comfortably with studies consider charge theory dynamic stochastic behavior.

5-Two regions of dielectric constant values are identified ($1 < D < 10$) and ($10 < D < 80$).

As it was expected, with increasing of dielectric constant of solvents and stability of DPPC and DMPC are increased also atomic charge of the some atoms were increased versus to increase of dielectric constant but some atoms were decreased.

Whit plot of the calculated energies, dipole moment and atomic charge of selected atoms of DPPC and DMPC as a function of $1/D$, we have linear equations and it is a good result. We propose for future is founding a empirical communicating between effect of solvent and membrane molecule.

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