

DFT-BASED COMPUTATIONAL INVESTIGATION ON FUNCTIONAL MONOMER AND SOLVENT SELECTION OF MOLECULARLY IMPRINTED POLYMERS FOR RECOGNITION OF CHLORPYRIFOS ORGANOPHOSPHATE INSECTICIDE

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Abstract

Density functional theory calculation was used to investigate the appropriate monomer and solvent for the preparation of chlopyrifos organophosphate molecularly imprinted polymers. The polymerization process of MIPs contained four essential elements, i.e. template, monomer, cross-linker and porogenic solvent. A computational chemistry was applied to optimize the polymerization system. Seven commonly used monomers, involving methacrylic acid, acrylic acid, acrolein, acrylonitrile, acrylamide, methacrylamide, and 4-vinylpyridine were studied. Stable complex interaction between chlopyrifos and monomer was chosen from the binding energies. Solvation effect was studied using the polarizable continuum model (PCM) for acetonitrile, tetrahydrofuran, toluene and dichloromethane. The appropriate monomer and solvent were selected from the results of the calculation and the most suitable solvent was chosen by the less effect on the interaction. The best pre-polymerization conditions are useful to synthesize MIPs for specific recognition of chlopyrifos organophosphate insecticide molecule.

Keywords: MIPs, Chlopyrifos, Quantum chemical calculation, DFT

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Introduction

Chlorpyrifos is the organophosphate pesticide introduced in 1965 by Dow Chemical Company. It acts on the nervous system of insects by inhibiting acetylcholinesterase. Chlorpyrifos used to kill a number of pest including insects, worms and beetle that is harmful to plants resulting in the increase of agricultural output. The uses of chlorpyrifos are of variety such as spraying in the soil, putting in the bottom of the hole, and injecting into the plant 's holes because of the insect (Shaolong *et al.*, 2017). Moreover, sometimes it used to treat seeds to defend the pest in the warehouse. For acute effects, the World Health Organization classified chlorpyrifos as Class II: moderately hazardous. The oral LD50 in experimental animals is 32 to 1,000 mg/kg. The dermal LD50 in rats is greater than 2,000 mg/kg and 1,000 to 2,000 mg/kg in rabbits. The 4-hour inhalation LC50 for chlorpyrifos in rats is greater than 200 mg/m³ (Michigan State University *et al.*, 2018).

Chlorpyrifos has used extensively more than 100 countries around the world to control insects in agricultural. Due to the toxicity of insecticides affecting the health of human, the residue in agriculture product is very important thing that should be study to control the effect of toxicity. Traditional detection methods are based on high cost instruments, such as high performance liquid chromatography coupled with photodiode array detector (HPLC-DAD), liquid chromatography-mass spectroscopy (LC-MS) (Idriss *et al.*, 2014) and gas chromatography-mass spectroscopy (GC-MS) (Ma *et al.*, 2013; Armstrong *et al.*, 2014). However, all these methods are laborious, time-consuming and requiring large of organic reagent. Therefore, simple technique with low cost and accurate analytical method are required.

Molecular Imprint is the powerful technique to analyze the small amount of the substance from the mixture. This technique produces the Molecular Imprinting Polymers (MIPs) with powerful ability of absorption with high sensitivity and selectivity including shape, size and functional groups of the imprinting sites to the template molecules. Moreover, the MIPs have high reusability with

low cost and easy preparation for various templates (Sushma *et al.*, 2013; Hai *et al.*, 2015; Xiaoping *et al.*, 2016). The principle of imprinting technique consists of template that is the target to be measured, functional monomer to be binding with the template, crosslinker to fix the template-monomer interaction in a high crosslink polymer matrix, initiator to initiate the polymerization process, and porogenic solvent to elute the target out of the polymer after preparation process.

Computational chemical calculation is a convenient and useful technique to predict the appropriate polymerization condition. Gaussian 09 program package was used to calculate electronic energy of molecular moieties. The result of calculation indicates the suitable condition with high reliability. A large number of published literatures showed that DFT is a precise and efficient algorithm to calculate hydrogen bond energy (Sushma *et al.*, 2013; Theeraphon *et al.*, 2013; Xiaoping *et al.*, 2016; Yi *et al.*, 2017). The value of binding energy (ΔE) is a crucial guideline for chosen appropriate monomer which the large energy presents the stronger interaction between template and monomer, meaning more beneficial to increase selective performance of MIPs (Idriss *et al.*, 2013; Sushma *et al.*, 2013; Matheus *et al.*, 2016; Yi *et al.*, 2017).

In this paper, the condition for MIPs were selected by using the density functional theory (DFT) method to calculate the binding energy between the monomer, crosslinker and template. Additionally, the organic solvent type was investigated to provide appropriate condition for MIPs synthesis. In the present work, condition for chlorpyrifos-MIPs i.e. monomer, crosslinker and solvent was studied. The effective procedure has useful to screening of component in other templates.

Experimental and Method

Computational Simulation

All computation calculations were performed utilizing Gaussian 09 program

(Shoulei *et al.*, 2007; Sushma *et al.*, 2013; Xiaoping *et al.*, 2016; Yi *et al.*, 2017;). Chemical structures of template, functional monomers (methyl methacrylate, acrylonitrile, methacrylamide, acrylic acid, acrolein, acrylamide and 4-vinylpyridine) and template-functional monomer complexes were assigned (Figure 1). Full optimizations were performed at the density functional theory level, using Becke's three-parameter Lee-Yang-Parr (B3LYP) and the 6-31G(d) basis set, in vacuum and solvation model (Theeraphon *et al.*, 2013; Xiaoping *et al.*, 2016). The energies of the template, monomers and complexes were obtained by the optimal conformation by the same method. Finally, the binding energies (ΔE) of template-functional monomer complexes were calculated using the following equation.

$$\Delta E_{(vacuum)} = E_{(complex)} - E_{(template)} - E_{(monomer)}$$

Where $E_{(complex)}$ is the interaction energy of the complex of monomer and chlorpyrifos in vacuum, and $E_{(template)}$ and $E_{(monomer)}$ are the energy levels of chlorpyrifos and monomer in vacuum, respectively.

Solvent effects were estimated using the polarizable continuum model (PCM) developed by Tomasi and coworker (Xiaoping *et al.*, 2016; Yi *et al.*, 2016). The calculations with solvation effect were performed at the density functional theory level using Becke's three-parameter Lee-Yang-Parr (B3LYP) and the 6-31G(d) basis set. The solvent effects of complexes were calculated from the equation

$$\Delta E_{(solv)} = E_{(solvent)} - E_{(vacuum)}$$

Where $E_{(solvent)}$ and $E_{(vacuum)}$ are the binding energies of complexes in solvent and in vacuum, respectively.

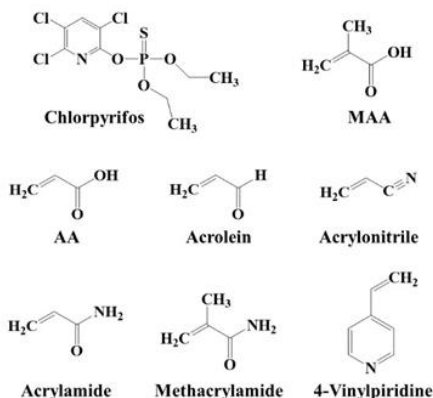


Figure 1. Chemical Structures of Template (chlorpyrifos) and Monomers

Results and Discussion

Computational chemistry had been demonstrated to be useful in elucidating the physicochemical properties of chemical entities that is pertinent for understanding the activity and chemical properties of imprinted system. The selection of appropriate monomer, crosslinker and porogenic solvent is an essential procedure in polymerization process of MIPs. In this work, a computational

Table 1. Binding energies for template, monomers and template-monomer complexes by DFT method at B3LYP level with 6-31G Basis Set in vacuum

Molecules	E (Chlorpyrifos/Monomer) (in hartree)	E (Monomer-Template) (in hartree)	kJ/Mol
Chlorpyrifos (Template)	-2750.22		
MAA	-306.49	-3056.72	-30.38
AA	-306.49	-3056.72	-30.00
Acrolein	-191.91	-2942.11	79.66
Acrylonitrile	-210.16	-2960.38	-7.60
Acrylamide	-247.30	-2997.53	-21.30
Methacrylamide	-286.62	-3036.85	-23.17
4-Vinylpyridine	-325.70	-3075.92	-11.94

* 1 hartree = 2625.5 kJ/mol.

approach was applied to optimize the polymerization system.

Optimization of Functional Monomer

Seven kinds of commonly used monomers were optimized to investigate the binding energy. The structures of template and monomers in this study are shown in Figure 1. From the Equation 1.1 the binding energy of monomers and chlorpyrifos are presented in the Table 1 : MAA (-30.38 kJ/mol), AA (-30.00 kJ/mol), Acrolein (79.66 kJ/mol), Acrylonitrile (-7.60 kJ/mol), Acrylamide (-21.30 kJ/mol), Methacrylamide (-23.17 kJ/mol), 4-Vinylpyridene (-11.94 kJ/mol)

The ΔE values with a given template are in the following order $\Delta E_{MAA} > \Delta E_{AA}$

$> \Delta E_{Methacrylamide} > \Delta E_{Acrylamide} > \Delta E_{4-Vinylpyridene} > \Delta E_{Acrylonitrile}$ except $\Delta E_{Acrolein}$ that are the positive value indicating

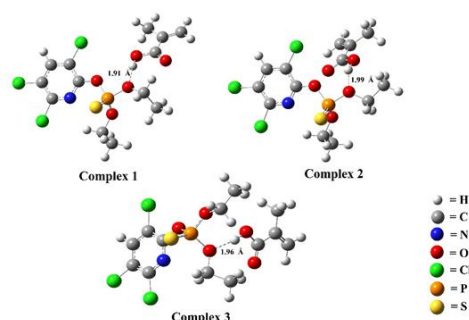


Figure 2. Possible interaction between Chlorpyrifos and Methacrylic acid

that the interaction cannot occur. From the calculation, the highest binding energy was presented in the complexes of MAA and chlorpyrifos template. Indicating interaction of MAA with template is stronger than another monomer, thus, MAA was chosen to study the possible interaction to the chlorpyrifos template in next section.

Possible Interaction Of MAA And Chlorpyrifos

The oxygen atom on chlorpyrifos acted as hydrogen bond acceptor by interacting with hydroxyl groups on MAA moieties. The possible interaction between MAA and Chlorpyrifos are shown in Figure 2. Chlorpyrifos-MAA complex 1 was found to afford the highest interaction energy of -30.38 kJ/mol, the bond distances of interacting atoms at the site of this interaction were 1.91, 1.99 and 1.96 Å for complex 1, 2 and 3, respectively. The interaction energies for chlorpyrifos-MAA complexes were -30.38, -27.70, -26.23 kJ/mol for complexes 1, 3, and 2 respectively. Such distances of complex 1 were found to be the least of all position, indicating that the hydrogen atom at hydroxyl groups on MAA presented the highest interaction energy (high negative energy) from hydrogen bonding in complex 1.

Selection of Solvent

The selectivity of molecular imprinted polymer affected by porogenic solvent. With chlorpyrifos as template and MAA as monomer, the $\Delta E_{(solv)}$ of four kinds of solvent with different dielectric constant were also

Table 2. Electric permittivity of four solvents and solvent energies for template–monomer complexes by DFT method at B3LYP Level with 6-31G Basis Set

Molecules	E (Chlorpyrifos/Monomer) (in hartree)	E (Monomer-Template) (in hartree)	kJ/Mol
Chlorpyrifos (Template)	-2750.22		
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*1 hartree = 2625.5 kJ/mol.

investigated by using the polarizable continuum model. From Table 2, the results showed a good correlation between dielectric constant and the $\Delta E_{(solv)}$ of the solvents (Xiaoping *et al.*, 2016). The solvation of chlorpyrifos with MAA monomer with higher dielectric constant had the higher $\Delta E_{(solv)}$. Toluene presented as optimal solvent due to it can dissolve both chlorpyrifos and MAA with the lowest $\Delta E_{(solv)}$. It was presented as the appropriate solvent for this preparation imprinting process of MIP system because the solvent with low $\Delta E_{(solv)}$ had less effect to interfered interaction between template molecule and monomer (Sushma *et al.*, 2013; Yi *et al.*, 2017).

Conclusions

In this work, the interaction energies between seven commonly used monomers complexing with chlorpyrifos template were investigated by computational calculation. The comparison of ΔE value of each complex was investigated to select the appropriate monomer for the template. MAA has chosen as the best monomer due to the highest binding energy with the template. The appropriate solvent for the MIPs synthesis was selected. Among the four studied solvents, toluene is the most suitable for chlorpyrifos imprinting process, with the minimum value of $\Delta E_{(solv)}$, the weakest interference in the self-assembly process between chlorpyrifos and MAA, and under this condition the imprinting polymers had more binding affinity and selectivity. This technique can be observed as a guideline for design and synthesis of MIPs with other templates.

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