Density Functional Theory (DFT) Study of Molecularly Imprinted Polymer (MIP) Methacrylic Acid (MAA) with D-Glucose

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Abstract. In order to find an alternative biosensor material which enables to detect the glucose level, therefore in this study, the interaction between Methacrylic Acid (MAA) based Molecularly Imprinted Polymer (MIP) with D-Glucose is investigated using the Density Functional Theory (DFT). The aim of this study is to determine whether a molecule of the MAA can be functioned as a bio-sensing of glucose. In this calculation, the Gaussian 09 with B3LYP and 631+G(d) basis sets is used to calculate all electronic properties. It is found that the interaction between a molecule of MAA and a molecule of D-Glucose was observed through the shortened distance between the two molecules. The binding energy of MAA/D-glucose and the Mulliken population analysis are investigated for checking possible interaction. From analysis, the MAA based MIP can be used as a bio-sensing material.


1. Introduction

Nowadays, diabetes becomes a major public health problem that can strike young ages people in the world. Diabetes is a disease which is caused when the system in the body cannot produce enough insulin. One of the factors of diabetes is high glucose level in blood which can be caused by heredity or unbalanced diet. In order to find an alternative biosensor material enabling to detect the glucose level, therefore in this study the interaction between Methacrylic Acid (MAA) based Molecularly Imprinted Polymer (MIP) with D-Glucose is investigated.

MIP is a polymer that has cavities in polymer matrix which is obtained through the molecularly imprinted technique. MIP technique is known as the very useful technique to design the receptors that will mimic some other molecules and recognize them [1,2]. The MIP purposed to make the template that will be able to recognize the target molecules. The mechanism of MIP technique is shown in Figure 1.

Figure 1 shows the process of MIP technique step by step. At first, template molecule and functional monomers are prepared to create functional monomer complex mediated by covalent and/or non covalent interaction during the polymerization process. During template extraction step, complementary recognition site are left the polymer and becomes the polymer matrix [1] [2] [4]. Thus, the target molecule will easily detach from the template and make MIP have high selectivity with other molecules [4-5].
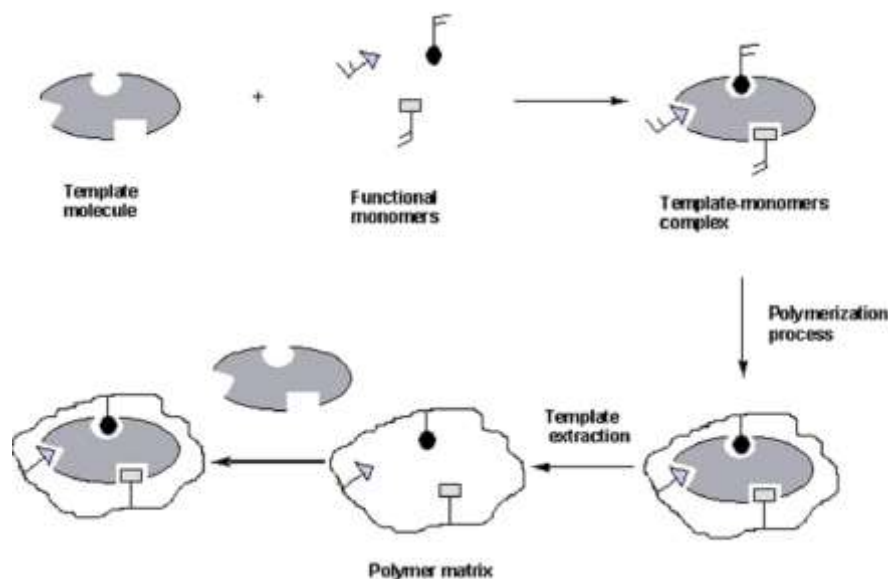
Figure 1. MIP technique scheme [3].

Methacrylic acid (MAA) is one of functional polymers that act as template molecule in MIP process. The MAA have been used due to its ability to take part in ion-ion, ion-dipole, dipole-dipole, Hydrogen, and Van Deer Waals interactions [6]. Furthermore, MAA is easy to have interaction with alkali molecules, hence, MAA can be used as template molecule and can have interaction with glucose. Here, glucose acts as a functional monomer.

2. Model and Computational Method

| | |
| (a) | (b) |
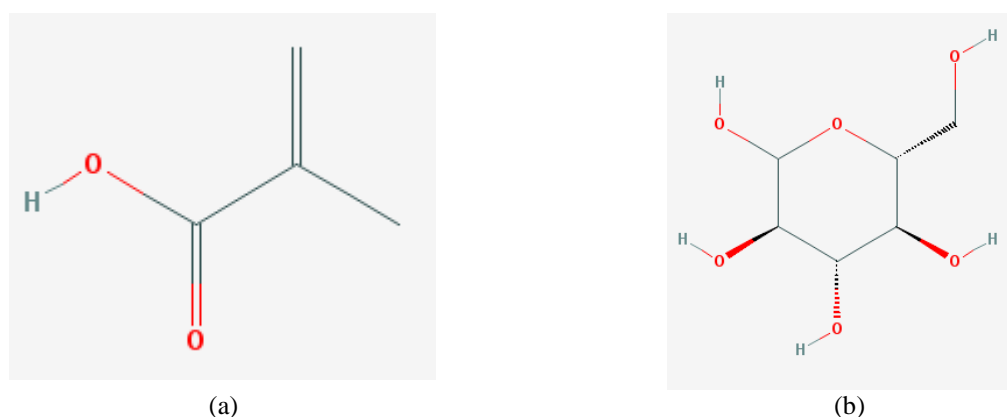
Figure 2. (a) The MAA structure [7]; (b) the D-Glucose Structure [8].

Figure 2, shows the structure of both MAA and D-Glucose. MAA is a clear colourless liquid or known as low-melting solid, vapour heavier than air, and may polymerize exothermically molecule [7]. The D-glucose is used as primary source of energy for organisms and naturally occurs in fruits and other parts of plant [8]. However, if the D-glucose or glucose is over consumed it will affect the human body health which is known as diabetes. Therefore, research related to MIP with functional monomer computationally and experimentally has been conducted. A computational approach using the Density Functional Theory (DFT) calculation and semi-empirical simulation have done to screening monomer for preparing MIP and to obtain the best monomer able to strongly interact with required functional

monomer [9-11]. Also, our previous work related to synthesis and characterization of MAA-based MIP with D-glucose template was done to seek the interaction of template and D-Glucose [12]. Therefore, to support our previous work [12] we present simulation on the interaction of MAA with D-glucose using DFT calculation.

The DFT methods have been carried out using the Gaussian 09 Program to calculate all electronic properties. For the molecular properties of both the Methacrylic Acid (MAA) and the D-Glucose molecules, the B3LYP/6-311+G(d) basis set is used. The cut-off energy was chosen based on the high accuracy precision mode applied in the calculation and the prediction change in energy was 2.55×10^{-8}. The energy of the system computed at RB+HF-LYP was -306.56 Hartree. The maximum force, the RMS force, the maximum displacement, and the RMS displacement was converged to reach a threshold value of 44×10^{-6}, 15×10^{-6}, 15.5×10^{-6} and 49.2×10^{-6}, respectively. The electron correlation is taken into account by using hybrid functional (B3LYP), that use the approximation from exact exchange from Hartree-Fock theory with exchange and correlation expressed through Kohn-Sham. Figure 3 shows the design of MAA and D-glucose molecule. A molecule structure of MMA (Figure 3a) consists of 12 atoms while a molecule structure of D-Glucose (Figure 3b) consists of 22 atoms. The optimization calculation has been done by completely relaxing all atoms without any symmetry constrain.
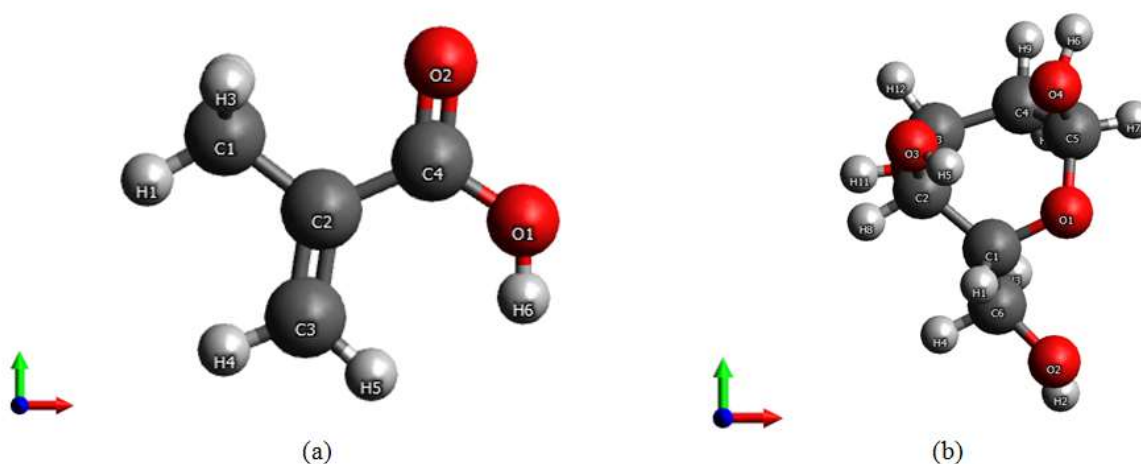
Figure 3. Design structure of (a) MAA (b) D-glucose.

3. Results and Discussion

In this section we present the results of the optimized geometry and the parameters related to the electronic structure of MAA and D-glucose. The optimization calculation was done by using B3LYP basis set, however for single molecule of both MAA and D-glucose the 6-311+G(d) basis set was used. The Optimization parameters are listed in Table 1.

Table 1. Optimization result parameters for MAA and D-glucose

Parameter	Maximum force	RMS Force	Maximum Displacement	RMS Displacement
MAA	0.000044	0.000015	0.001515	0.000492
D-Glucose	0.000044	0.000015	0.001515	0.000492
Threshold	0.00045	0.0003	0.0018	0.0012

Table 2. Total Mulliken charge between MAA and D-glucose after optimization calculation

Atom Label	Mulliken Charge	Atom Label	Mulliken charge
C1	-0.11717	O19	-0.00586
C2	0.294533	O20	0.004427
H3	0.007057	H21	0.026242
H4	0.029586	H22	-0.00368
H5	0.00355	O23	-0.00176
C6	-0.05226	C24	-0.0164
H7	0.008824	H25	0.003561
H8	0.001928	C26	-0.09627
C9	-0.1692	C27	0.062832
O10	0.032911	H28	-0.00717
H11	0.000272	H29	-0.00205
O12	-0.02275	O30	0.02089
O13	0.022566	C31	-0.00514
H14	-0.01351	H32	-0.0063
H15	-0.00699	H33	0.004014
H16	-0.00647	H34	0.01065
C17	-0.00881	H35	-0.00872
C18	0.016667		

From Table 1, we acquire that the convergence criteria are already met since the value of each parameters (maximum force, RMS force, maximum displacement, and RMS displacement) are lower than threshold. Hence, we can say that the MAA and D-Glucose molecule are already optimized by using B3LYP/6-311+G(d) basis set. After the optimization process, the structure of MAA and D-Glucose does not change; this can be seen from Figure 4. The shape of MAA structure is still planar after optimization (Figure 4a). The bonding within D-Glucose seems very tight because it has double bond within its structure and hence the shape of D-Glucose does not change as well.
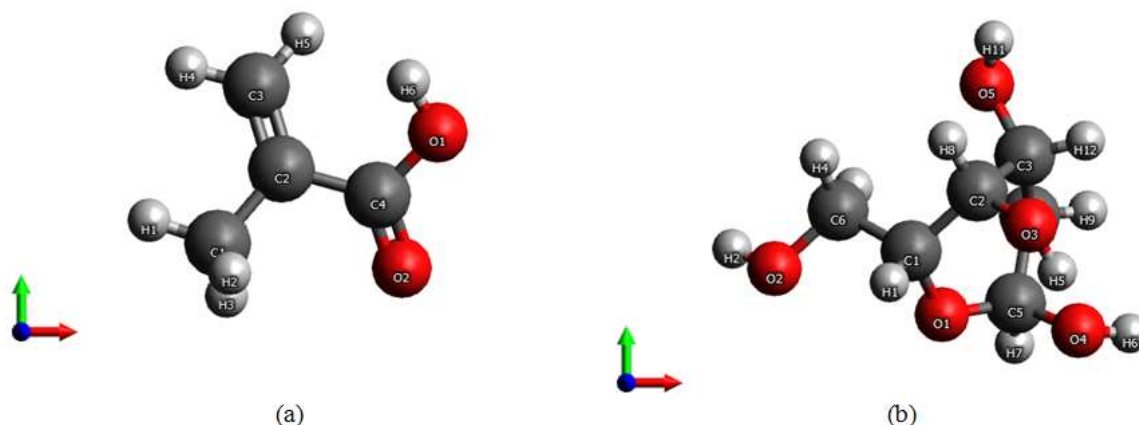
Figure 4. The optimized structure of (a) MAA and (b) D-glucose.

Next is the calculation of MAA and D-glucose interaction. The initial design of MAA and D-Glucose is depicted in Figure 5. Interaction between MAA and D-Glucose can be checked from their distance. At this point, our reference distance between 2 molecules of MAA and D-glucose is taken

from C2-C6 initial distance that is 5.65 Å (see Figure 5). The C2 atom belongs to MAA while C6 atom belongs to D-glucose. The selection of mentioned atoms is based on the center of each molecule and to make the measurement easier to do.

After the optimization process, the distance between MAA and D-Glucose increases by 0.85 Å that is change from 5.65 Å to 6.41 Å. The change in distance shows that there are some forces, called as the non covalent interaction, that make MAA and D-Glucose repels each other. However, if we look into Figures 5 and 6, the distance between O2 in MAA and O4 in D-glucose are getting closer. The O2-O4 distance is decreased by 3.815 Å that is change from initially 6.62 Å to 2.81 Å. It is shown that the non covalent interaction occurred. In addition, the hydrogen bonding between O2 and O4 observed, meaning that the MAA and D-glucose interaction occurred.

The interaction between MAA and D-Glucose can also be observed from the total Mulliken charge. Once we have optimized structure, we can not only depend on position but also the electronic density. The fastest and easiest way to see the density is through the Mulliken charges population. Table 2 shows the total Mulliken charge of MAA- D glucose structure. The sum of Mulliken charge is not 0, but they still have the charge between them. Despite the Mulliken charge which is the easiest way to analyse the interaction, it very depends on the basis set. We cannot, therefore, depend only on Mulliken population analysis. The other way to see the interaction between 2 molecules is through binding energy (ΔE_{bind}).

The formulation of binding energy used is $\Delta E_{bind} = E_{complex} - (E_{MAA} + E_{D\text{-}glucose})$. Using 6-311+G(d) basis set, the ΔE_{bind} between MAA and D-glucose is strong that is -2143.927 a.u.

From the 3 (three) ways of checking the interaction between MAA-D glucose: bonding interaction, Mulliken population analysis, and binding energy, we can see that MAA interacts with D-glucose. Hence, MAA based MIP can be used as a sensor to sense the D-Glucose. The D-Glucose will fill the cavity in the template because MAA will attract them to fill the cavity. From the chemical reaction point of view, the interaction between MAA and D-Glucose does not form chemical reaction, so it can be easily removed from the template.
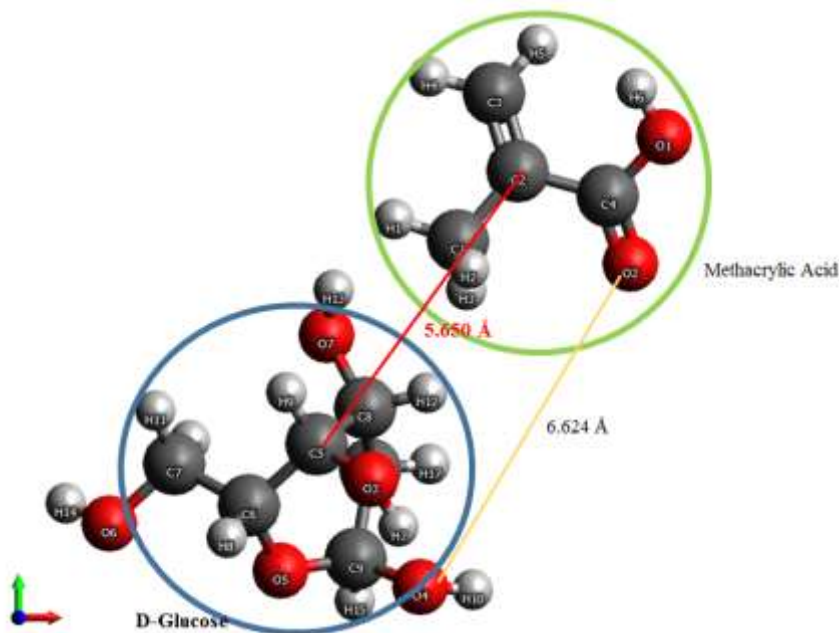
Figure 5. The initial structure of MAA-D glucose before optimization calculation.
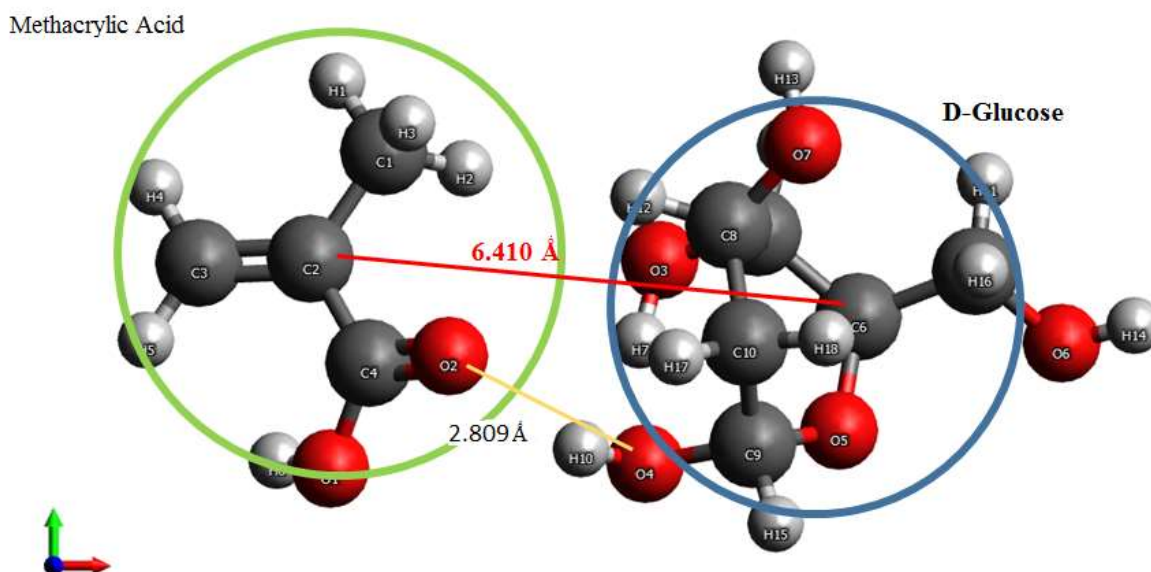
Figure 6. The optimized structure of MAA - D glucose.

4. Summary

The calculation of MAA based MIP interactions with D-glucose using the density functional theory (DFT) was done to study the structure and electronic properties of MAA/D-glucose for diabetes application. The interaction of a molecule of MAA and a molecule of D-glucose is non covalent interaction. The Mulliken population analysis and binding energy calculation also shows that both MAA and D-glucose are having interaction one another though a single MAA molecule is presented, there still interaction can be observed. From this study, MAA based MIP is possible to be used as a glucose sensor.

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