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Preliminary Studies of the Effect of Recognition Layer's Length in Electrochemical DNA Sensor

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Abstract: ***DNA-based electrochemical sensing can promise a simple, accurate and inexpensive for disease diagnosis. One of the main parts in this type of DNA sensor is linker or recognition layer. This study focuses on preliminary approach towards the effect of the linker in DNA sensor. A theoretical approach has been carried out to four different lengths of linker which involve Schiff base molecules with different R group attached ro the molecule (3,6,9, and 12 carbon chain). This study has been carried out using density functional theory (DFT) bu using GAUSSIAN 09 software package with the standard 6-31G9(d,p) basis set for all the calculations. Structure drawing was done with Gauss View 5.0. Energy, dipole moment, HOMO, LUMO, hardness (□), softness (□) and energy gap were calculated. Results showed that the length of the linker does not play a role in this study. The best results obtained was from 6 carbon length as it has the highest value of dipole moment which is 4.1622 and the lowest energy gap of 3.13 eV among the other chain. This theoretical result will be compared with experimental results in the near future.***

Index Terms: ***DNA Sensor, Linker in Electrochemical DNA Sensor, Density Functional Theory,***

I. INTRODUCTION

Schiff base compound is known for its low-cost preparation and normally formed by the condensation reaction of ketones or aldehydes with primary amines [1-3]. Schiff base compound has been extensively applied in pharmaceutical and biological studies [4]. This has sparked our interest to apply Schiff base compound as a linker in DNA electrochemical sensor with four different alkyl chain as the R group.

There are many methods to detect DNA. electrochemical DNA sensor is the easiest, sensitive and selective method reported so far [5]. However, a suitable linker or also know as recognition layer is needed to be attached to a suitable substrate such as gold, platinum, silver or indium tin oxide (ITO). Furthermore, DNA probe must be sufficiently immobilised [6]. All molecular-based biosensors rely on highly specific recognition events which typically involve probe sequence immobilised within the recognition layer. The length of linker may also affect DNA immobilisation.

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Reaction scheme for Schiff base molecules derivatives can be seen in Figure-1. COOH group will bind with the gold surface substrate while the other R group will bind directly with phosphate group from DNA. Phosphate group involved normally taking consideration with all four nucleotides which are adenosine, cytidine, guanosine and thymidine. Since this is preliminary studies, this paper only reported on the adenosine part. Other nucleotides will be reported in the near future. Figure 2 shows the complete Schiff base derivatives attached to adenosine via the oxygen atom. One side of R group will be attached to the substrate while the other R group is attached to adenosine nucleotide. This side of R group has been varied the length which involves carbon chains that are 3, 6, 9 and 12 carbon chains to see the effect of recognition length towards the effectiveness of DNA detection.

II. COMPUTATIONAL METHOD

Structure drawings were done using GaussView 5.0 and all calculations were performed with Gaussian 09 software package program [7]. There are many computational chemistry methods as well as theoretical studies about the determination of biological activity of chemical activity [8], [9]. Quantum-chemical descriptors are very suitable to determine the ranking biological activity. Quantum-chemical descriptors are very suitable to determine the ranking biological activity. These parameters are the highest occupied orbitals (HOMOs) and the lowest unoccupied molecular (LUMOs), the energy gap between LUMO and HOMO (ΔE_{GAP}), dipole moment (μ), hardness (η) and softness (σ). To analyse these biological activity ranking one of the density functional theory (DFT) methods, named Becke, 3-parameter, Lee-Yang-Parr (B3LYP) was selected and the rest of the atoms were selected as basis sets. The calculation to determine the biological activity were calculated by using Eqs 1-4.

$$\Delta E_{GAP} = E_{LUMO} - E_{HOMO} \quad (1)$$

$$\mu = (E_{HOMO} - E_{LUMO}) / 2 \quad (2)$$

$$\eta = (E_{LUMO} - E_{HOMO}) / 2 \quad (3)$$

$$\sigma = 1 / \eta \quad (4)$$

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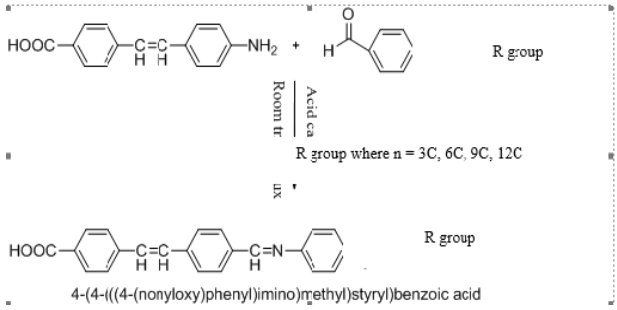

Figure 1. Reaction scheme to synthesise Schiff base molecules with various R group which involve 3, 6, 9 and 12 carbon chain

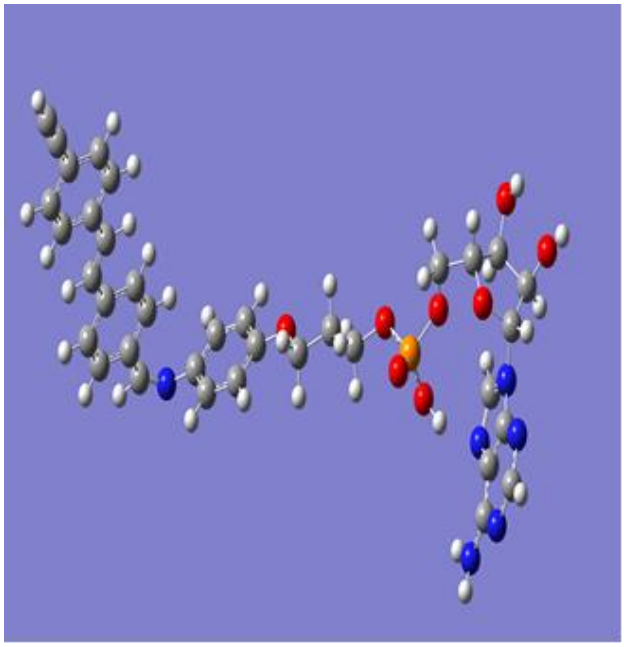

Figure 2. The overall molecule of Schiff base derivatives bind with adenosine with 2 R groups, COOH (fixed) and carbon chain length varied to 3C, 6C, 9C and 12C.

III. RESULTS AND DISCUSSION

All calculated parameters are represented in Table 1. In computational chemistry, normally Hartree-Fock (HF) is used as a method of approximation for the determination of the wave function and the energy of a quantum in a stationary state. HF is also known as self-consistent field method (SCF) assuming each particle is subjected to the mean field created by all other particles. E_{SCF} in table 1 shows the central starting point for most methods that describe the many-electron system more accurately.

HOMO is an important quantum chemical descriptor and mainly associated with electron donating ability of molecule. The higher the value of HOMO, the higher the tendency of electron transfer to acceptor molecule [10]. The ranking of the biological activity of the derivatives are as follows:

$(CH_2)3 > (CH_2)9 > (CH_2)12 > (CH_2)6$

While the low LUMO value indicates that the electron-accepting ability of the molecules is higher. The binding ability of the compounds are:

$(CH_2)3 > (CH_2)12 > (CH_2)9 > (CH_2)6$

It can be seen that from the energy gaps (E_{GAP}) between HOMO and LUMO for the compounds are as follows:

$(CH_2)3 > (CH_2)9 > (CH_2)6 > (CH_2)12$

The lower value of the E_{GAP} explains the eventual charge transfer interaction taking place within the molecules. The lower value of this descriptor shows that the molecule is more active [10].

On the other hand, chemical hardness (η) is associated with the stability and reactivity of a chemical system.this descriptor measures the resistance to change in the electron distribution or charge transfer. Hard molecules have a big E_{GAP} value and of molecules have small E_{GAP} [9], [10]. Biological molecules are known as of molecules. This means that soft molecules can easily interact with biological molecules or human body. Biological activity is proportional to the increase of the softness value and vice versa. Based on the softness values obtained, the sequence of biological activity are:

$(CH_2)3 > (CH_2)9 > (CH_2)6 > (CH_2)12$

Another important descriptor is electronic chemical potential (μ) also known as dipole moment which is defined as the negative of electronegativity of a molecule. Based on the biological activity obtained the ranking for dipole moment of the molecules are:

$(CH_2)6 > (CH_2)12 > (CH_2)3 > (CH_2)9$

Table 1. Calculated quantum chemical descriptors at B3LYP method

	$(CH_2)3$	$(CH_2)6$	$(CH_2)9$	$(CH_2)12$
E_{SCF} (au)	-2664.6088	-2782.5581	-2900.5080	-3018.4574
HOMO (eV)	-0.19381	-0.19161	-0.19174	-0.19144
LUMO (eV)	-0.07719	-0.07655	-0.07667	-0.07673
E_{GAP} (eV)	3.1734	3.1309	3.1312	3.1214
μ (eV)Dipole moment	1.8296	4.1622	1.7605	3.959
η (eV)Hardness	0.05831	0.05753	0.05754	0.05735
σ (eV^{-1})Softness	17.1497	17.3822	17.3807	17.4353

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Based on all biological activity obtained, the optimum recognition layer can be seen at Schiff base molecules with 6 carbon chains attached to adenosine. This preliminary result indicates that there is a certain length which is suitable towards the electrochemical DNA system. The future experimental study will be carried out to be compared with theoretical results obtained.

IV. CONCLUSIONS

DFT is a promising tool to study theoretical aspect of recognition layer's length in electrochemical DNA sensor. From the value of biological activities obtained the length of recognition layers does not play a significant role. The best length obtained was from Schiff base molecules with 6 carbon chain group attached to adenosine. However further study considering other nucleotides which are cytidine, guanosine and thymidine will be further investigated. Furthermore, experimental work will be carried out by synthesizing all the molecules involved to be compared with theoretical results.

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