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On the molecular modeling analyses of the interaction between nano zinc oxide and bacteria

Noha M. Sabry [1], Sahar T. M. Tolba [2], Fagr Kh. Abdel-Gawad [1], Samah M. Bassem [1], Hossam Nassar [3], Gamila E. El-Taweel [1], Medhat A. Ibrahim [4, *]

[1]Environmental Research Division, Centre of Excellence for Advanced Science, National Research Centre, 33 El-Bohouth St., 12622 Dokki, Giza, Egypt
[2]Department of Microbiology, Faculty of Science, Ain Shams University, Cairo, Egypt
[3]Environmental Sciences and Industrial Development Department, Faculty of Postgraduate Studies for Advanced Sciences (PSAS), Beni-Suef University, Beni-Suef, Egypt
[4]Spectroscopy Department, National Research Centre, 33 El-Bohouth Str. 12622 Dokki, Giza, Egypt

*corresponding author e-mail address: ***medahmed6@yahoo.com***

ABSTRACT

A model molecule for bacteria is built to study the possible interaction between nano ZnO and bacteria. Total dipole moment, HOMO/LUMO band gap energy and molecular electrostatic potential ESP are calculated at B3LYP/6-311G(d,p) level of theory. Oxygen of dehydarated ZnO ($ZnO.2H_2O$) weakly interacts through hydrogen bond of COOH, NH_2 of protein. Results indicated that interaction throughout COOH is most probable as its highly reactive in terms of total dipole moment (9.5901 Debye) and lower HOMO/LUMO band gap energy (1.5146 eV).

Although another scheme is tried whereas COOH and ZnO interacts through the complex state with the release of OH radical while its least probate in terms of the calculated physical properties. ESP results confirm that ZnO in nanoscale could act as sensor for bacteria.

Keywords: *ZnO; Protein; Bacteria; B3LYP/6-311G(d,p).*

1. INTRODUCTION

Nanoscale materials have emerging applications in many fields according to their significant physical, chemical, and biological properties [1-3]. Biological activity of some nanomaterials especially nano metal oxides such as ZnO dedicate it for many applications. Although the ZnO in bulk structures show an antimicrobial activity in the mid of 20th century [4]. The beginning of application of ZnO in nanoscale range is started by the end of the century around 1995, it was utilized as an antimicrobial agent by Sawai et. al. [5-6]. It is stated that the activity of ZnO is depending on the grain size, while decreasing the size is increasing the surface area of a given nanoscale metal oxide. For ZnO it is indicated that, its antibacterial activity is affected by its surface area, which related to the grain size, while it is indicated experimentally that little effect is noticed as a function of crystalline structure and particle shape [7]. The most important aspect which increases the demand for nanoscale ZnO as antibacterial agent its wide applications for both Gram-positive and Gram-negative bacteria [8-9]. It could be described and categorized among the best antibacterial agents [10]. Many researchers reported that although the antibacterial activity of ZnO is observed the mechanism of which is still not known [11]. ZnO show antibacterial activity against *E. coli* [12]. Later on its shows also antibacterial activity against *Pseudomonas aeruginosa* isolates of burn infections [13]. Nano ZnO also shows antibacterial activity against Aeromonas hydrophila [14]. It is indicated that as the size decreased the inhibition is increased. As an attempt to present a mechanism, it could be concluded that, there is ability of generating reactive oxygen species according to the high surface area and the existence of surface defects. ZnO in nanoscale could interact with bacterial cell membrane which makes structural changes, this in turn may reduce the surface of the cell leading to degradation and subsequently cell death [15]. In our previous work, molecular modeling and/or molecular modeling with molecular spectroscopy are tools for understanding the mechanism of interaction in many systems especially in the biological systems. Recently molecular modeling was confirming experimental tools to understand some interactions. For understanding the interaction between metal oxides and amino acids [16]. To explain the interaction between organic structures such as dioxin and fish in marine environment [17]. To elucidate the vibrational, structural parameters for some 5-Chloro-2-methoxy-N-phenylbenzamide derivatives [18] the overall aim is to functionalize their application in biomedical field. Another application which is also based on the interaction between ZnO and bacteria is its application as sensor, In which ZnO is decorated with gold then tested effectively as sensor for bacterial DNA hybridization [19]. ZnO in the form of nanowire is fabricated and tested as sensor for biomolecules such as protein [20]. ZnO is further modified with reduced graphene oxide to act as sensor for amino acids [21]. Recently, many research papers reported that ZnO is still utilized as it is and/or as composite to enhance its ability and activity as antibacterial agent against wide range of bacteria [22-29]. Molecular modeling shows many level of theories could be applied to investigate the electronic properties of ZnO as well as its composites [30-32].

In this work, molecular modeling at B3LYP/6-311G(d,p) to describe the type of interaction between nano ZnO and amino acid. The amino acid here is proposed as a building block for protein structure representing bacteria. The interaction is described in terms of the calculated total dipole moment, HOMO/LUMO band gap energy and molecular electrostatic potential ESP.

2. EXPERIMENTAL SECTION

All the studied structures are calculated with Gaussian 09 [33] program at Spectroscopy Department, National Research Centre, Egypt.

3. RESULTS AND DISCUSSIONS

3.1. Building model molecules. ZnO is prosed to hydrate with two water molecules as indicated in figure 1-a. the interaction between ZnO and bacteria is supposed to take place through the hydrogen bonding of active sites of protein (COOH and NH_2).

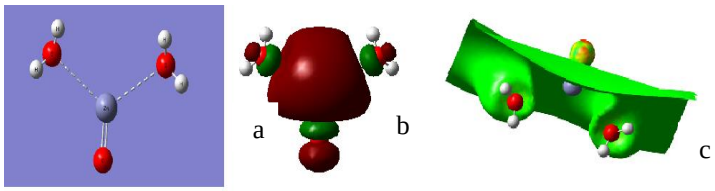

Figure 1. B3LYP/6-311G(d,p) optimized structure of a- $ZnO.2H_2O$; b- HOMO/LUMO band gap energy of $ZnO.2H_2O$ and c- Molecular electrostatic potential ESP of $ZnO.2H_2O$.

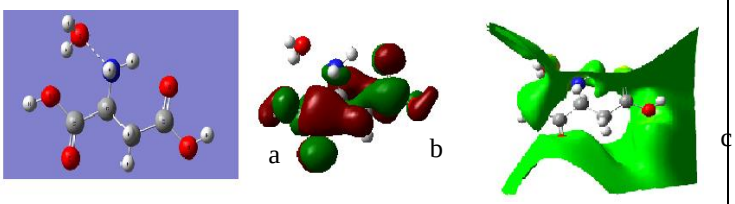

Figure 2. B3LYP/6-311G(d,p) optimized structure of a- amino acid monohydrate; b- HOMO/LUMO band gap energy of amino acid monohydrate and c- molecular electrostatic potential ESP of amino acid monohydrate.

Accordingly, a model for protein structure is indicated as shown in figure 2-a. For the interaction between ZnO and protein, there are two possibilities the first one is through weak interaction between ZnO and H of COOH as indicated in figure 3-a. Another possibility of interaction is through the H oh NH_2 as indicated in figure 4-a.

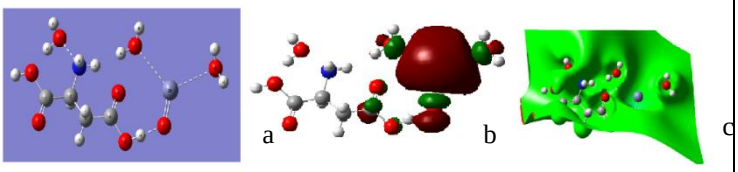

Figure 3. B3LYP/6-311G(d,p) optimized structure of a- amino acid monohydrate/ $ZnO.2H_2O$; b- HOMO/LUMO band gap energy of amino acid monohydrate/ $ZnO.2H_2O$ and c- molecular electrostatic potential ESP of amino acid monohydrate/ $ZnO.2H_2O$. The interaction took place through COOH.

It is worth to point out that for the first scheme indicate in figure 3-a dehydrated ZnO is interacted with monohydrated protein whereas the water molecule is located on the amid group. In the other scheme, the dehydrated ZnO interacts also with monohydrated protein whereas water is located at COOH as shown in figure 4-a.

B3LYP/6-311G(d,p) [34-36] model is utilized to calculate total dipole moment, HOMO/LUMO band gap energy and molecular electrostatic potential.

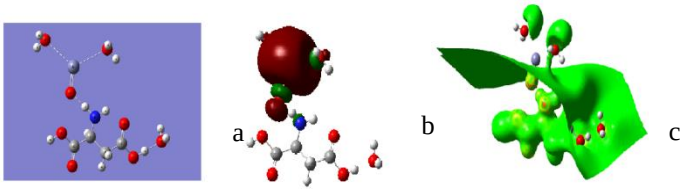

Figure 4. B3LYP/6-311G(d,p) optimized structure of a- amino acid monohydrate/ $ZnO.2H_2O$; b- HOMO/LUMO band gap energy of amino acid monohydrate/ $ZnO.2H_2O$ and c- molecular electrostatic potential ESP of amino acid monohydrate/ $ZnO.2H_2O$. The interaction took place through NH_2.

3.2. Calculated physical parameters. To describe the interaction between the metal oxide and protein three important physical parameters are calculated the total dipole moment, which listed in table 1. HOMO/LUMO band gap energy, which is listed in table 1 and indicated in figure 1-b, 2-b, 3-b, 4-b. Finally, the molecular electrostatic potential ESP which is mapped in figures 1-c, 2-x, 3-c, 4-c respectively.

Total dipole moment and HOMO/LUMO band gap energy is an indication for chemical and biological reactivity of given chemical compounds [37-38]. For reactive compounds, their total dipole moment increases which their band gap energies decrease. Regarding table 1, $ZnO.2H_2O$ shows total dipole moment of 8.6662 Debye while band gap energy is 2.5285 eV. For the model molecule of protein, the total dipole moment is 1.1890, the band gap is 2.8281 eV. As far as $ZnO.2H_2O$ interacts with protein the total dipole moment is increased to 9.5901 Debye while band gap energy is sharply decreased to be 1.5146 eV for the scheme of interaction through COOH as indicated in figure 3-b

Molecular electrostatic potential ESP of the given structures can be displayed as the charge distribution revolving around the given structure in space. It is an important parameter for understanding both the electrophilic and nucleophilic attacks sites especially for biological recognition [39] this is of course for biological interactions process. More general, it could be a good description for hydrogen bonding interactions [40]. In the present work, the mapping of the ESP is indicated in figures 1-c, 2-c, 3-c, 4-c respectively.

To describe the figures of ESP contours, the different values of the electrostatic potential at the surface are represented by different colors. Potential is following the increasing orders: red < orange < yellow < green < blue. Where blue indicates the highest electrostatic potential energy and red indicates the lowest electrostatic potential energy [41]. Intermediary colors represent intermediary electrostatic potentials. As it can be seen from the ESP maps, the negative regions are mainly centralized on the O indicating possible sites for electrophilic attacks. Whereas the maximum positive region is localized over the Zn atoms indicating

possible sites for nucleophilic attacks. These data confirm those obtained with total dipole moment and HOMO/LUMO band gap energy. The ZnO is an active surface for interaction with protein throughout COOH and/or NH_2.

The existence of a high surface area of ZnO in nanoscale with defects as indicated in the ESP contour could be the reason for the interaction between ZnO and the protein structure even in bacteria.

The overall change in the studied physical properties under the interaction between the studied surfaces dedicates ZnO to act as a sensor for bacteria.

Correlating the schemes of interactions between ZnO and studied model protein structure revealed that interaction through COOH expanses of lower energy than that for NH_2 and considered more reactive in terms of the total dipole moment values.

Another interaction is tried for the most probable interaction indicated in figure 3, interaction through COOH. The interaction is repeated at the same level of theory as the complex state as shown in figure 5-a, 5-b, and 5-c respectively.

As listed in table 1, the total dipole moment is 5.6706 Debye while the HOMO/LUMO band gap energy is 1.5209 eV. In this interaction, the metal oxide iinteracts with carboxyl group through Hydrogen bonding with the release of OH group as shown in figure 5-a. These in terms of the total dipole moment are less reactive than adsorb state interaction also throughout COOH. Even the band gap energy (1.5209eV) is slightly higher that adsorb state (1.5146 eV).

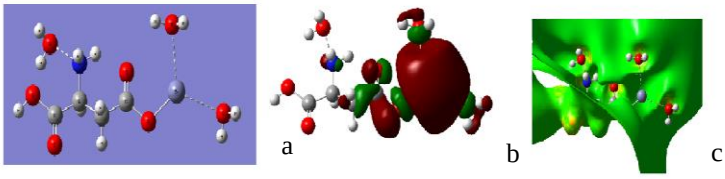

Figure 5. B3LYP/6-311G(d,p) optimized structure of a- amino acid monohydrate/ $ZnO.2H_2O$; b- HOMO/LUMO band gap energy of amino acid monohydrate/ $ZnO.2H_2O$ and c- molecular electrostatic potential ESP of amino acid monohydrate/ $ZnO.2H_2O$. The interaction took place through COOH. The interaction is complex not adsorb state.

Table 1. B3LYP/6-311G(d,p) calculated total dipole moment as Debye, HOMO/LUMO band gap energy as eV for the studied structures.

Structure	Total dipole moment	Band gap energy
$ZnO.2H_2O$	8.6662	2.5285
Amino acid monohydrate	1.1890	2.8281
Amino acid monohydrate/ $ZnO.2H_2O$ (COOH)	9.5901	1.5146
Amino acid monohydrate/ $ZnO.2H_2O$ (NH_2)	8.9878	2.2749
Amino acid monohydrate/ $ZnO.2H_2O$ (COOH) Complex	5.6706	1.5209

4. CONCLUSION

Nano ZnO physical properties are changed as far as it interacts with the protein model molecule representing bacteria. Accordingly, O could be a sensor for bacteria. The mechanism of sensing is depending on the adsorb or complex interactions between the hydrogen of NH_2 and COOH and the oxygen of the ZnO molecule. As adsorb state weak interaction took place between oxygen and hydrogen of NH_2 and COOH separately. The total dipole moment and HOMO/LUMO band gap energy indicate that interaction as adsorbs state with COOH is more likely than that with NH_2. For the complex state, the interaction is tried with COOH with the release of free radical OH in terms of HOMO/LUMO energy and total dipole moment this interaction is less like to happen as compared with that of adsorbing state throughout the same site.

It could be concluded from the molecular electrostatic potential that ZnO offers a high surface area with defects which enable the protein of bacteria to be electrostatically bonded (weak or adsorb state) with ZnO.

This interaction makes ZnO is a good sensor for bacteria in one hand and could be also an explanation for the bioactive behavior of nanoscale ZnO against bacteria.

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