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**ORIENTAL JOURNAL OF CHEMISTRY**
An International Open Free Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2015, Vol. 31, No. (3):
Pg. 1509-1513

# Quantum Mechanical Study on the Adsorption of Drug Gentamicin onto γ-$Fe_2O_3$ nanoparticles

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http://dx.doi.org/10.13005/ojc/310329

(Received: June 27, 2015; Accepted: August 03, 2015)

**ABSTRACT**

In this work, using quantum mechanics, the interaction of drug gentamicin with ã-$Fe_2O_3$ nanoparticles have been studied. $Fe_2O_3$ nanoparticles were modeled using $Fe_6(OH)_{18}(H2O)_6$ ring clusters. gentamicin molecule can coordinate to the γ-$Fe_2O_3$ nanoparticles via its own OH or $NH_2$ groups. All of the calculations have been performed using a hybrid density functional method (B3LYP) in solution phase. Three possible modes of noncovalent interaction of gentamicin onto ã-$Fe_2O_3$ nanoparticles were investigated. Quantum molecular descriptors in the drug-nanoparticle systems were studied. It was found that binding of gentamicin with γ-$Fe_2O_3$ nanoparticles is thermodynamically favorable. Among NCOOH and NCOCl, the first one has more binding energy and can act as a suitable system for drug gentamicin delivery within biological systems (noncovalent). Gentamicin can intract with γ-$Fe_2O_3$ nanoparticles via OH and $NH_2$ groups which the first one has more binding energy.

**Key words**: Gentamicin, γ-$Fe_2O_3$ nanoparticles, DFT, Drug delivery, Quantum molecular descriptors.

## INTRODUCTION

Gentamicin is a commonly used antibiotic which prevents bacterial infection around the implant. It is an aminoglycoside antibiotic, and can treat many types of bacterial infections, particularly Gram-negative infection. It is also one of the few heat-stable antibiotics that remains active even after autoclaving, and this makes it particularly useful in the preparation of certain microbiological growth media[1].

Regarding the increasing use of nanotechnology in today's life, understanding of the functional mechanism of nanoparticles is of great importance. The rapid development of nanoscience has opened new ways in timely and prompt diagnosing of diseases and drug delivery. The use of nanoparticles in drug delivery is a new field which is rapidly developing[2-5].

Jayarathne et al. presented a model for γ-$Fe_2O_3$ nanoparticles on the basis of $Fe_6(OH)_{18}(H_2O)_6$ ring cluster which is in good consistency with the experimental data including vibration frequencies and bond lengths[6]. The huge surface, easy separation and low cost are the reasons to use γ-$Fe_2O_3$ nanoparticles as the strong adsorbent materials.

In spite of extensive use of magnetic nanoparticles, so far, molecular mechanism of adsorption of drugs in water by these nanoparticles has not been investigated. In this work, using quantum mechanical methods, the noncovalent adsorption of gentamicin onto γ-$Fe_2O_3$ nanoparticles was studied.

**Computational details**

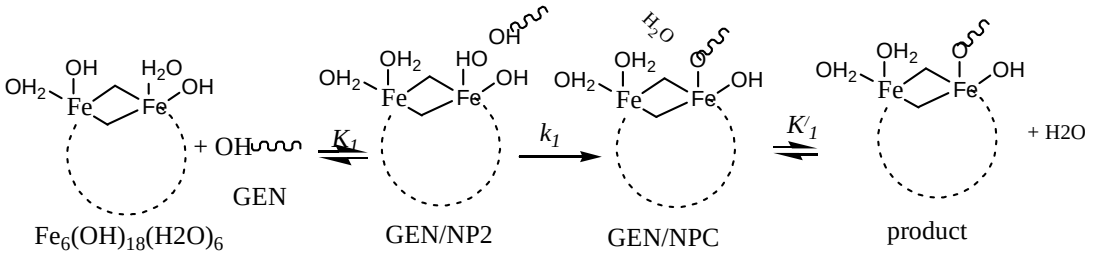
All of the present calculations have been performed with the B3LYP[7-9] hybrid density functional level using the GAUSSIAN 03 package[10]. The 6-31G(d,p) basis sets were employed except for Fe where the LANL2DZ basis set was used with effective core potential (ECP) functions.

The solvent has an important role in chemical reactions explicitly or implicitly[11-15]. The implicit effects of the solvent was considered by using the polarized continuum model (PCM)[16]. In the PCM method, the molecular cavity is made up of the union of interlocking atomic spheres. All degrees of freedom for all geometries were optimized in solution (water).

## RESULTS AND DISSCUSSION

The properties of γ-$Fe_2O_3$ nanoparticles were modeled using $Fe_6(OH)_{18}(H_2O)_6$ ring clusters of six edge sharing octahedra joining via 12 OH groups. The 6 water molecules and 6 surface OH groups were expected to form a network of H-bonded interactions (Fig. 1). The optimized geometries of gentamicin (GEN), $Fe_6(OH)_{18}(H_2O)_6$ or **ã**-$Fe_2O_3$ nanoparticle (NP) in solution phase are shown in Fig. 1. Gentamicin is a non-planar molecule with the amino and hydroxyl groups protruding out of the molecular plane as shown in Fig. 1.

Three possible modes of noncovalent interaction of Gentamicin onto γ-$Fe_2O_3$ nanoparticles were studied. Figures 2-4 present these configurations in solution phase, namely, GEN/NP1-GEN/NP3. Gentamicin may interact with γ-$Fe_2O_3$ nanoparticles through amino ( GEN/NP1 ) and hyroxyl (GEN/NP2) groups to form hydrogen bonds. In GEN/NP3 parallel orientation was considered.




**Scheme 1**

**Table 1: Bonding energies (kJ/mol) quantum molecular descriptors (eV) for optimized geometries**

| Species | $E_b$ | $E_{HOMO}$ | $E_{LUMO}$ | $E_g$ | I | A | μ | η | ω |
|---|---|---|---|---|---|---|---|---|---|
| GEN | - | -5.95 | -1.85 | 4.11 | 5.95 | 1.85 | -3.90 | 2.05 | 3.70 |
| NP | - | -5.58 | -4.48 | 1.10 | 5.58 | 4.48 | -5.03 | 0.55 | 22.95 |
| GEN/NP1 | -74.61 | -5.93 | -4.33 | 1.60 | 5.93 | 4.33 | -5.13 | 0.80 | 16.39 |
| GEN/NP2 | -94.35 | -6.09 | -3.30 | 2.79 | 6.09 | 3.30 | -4.69 | 1.40 | 7.88 |
| GEN/NP3 | -86.82 | -5.94 | -3.27 | 2.67 | 5.94 | 3.27 | -4.60 | 1.33 | 7.94 |

The binding energies ($E_b$) of gentamicin whit γ-$Fe_2O_3$ nanoparticles are calculated using the following equation and presented in Table 1:

$$E_b = E_{GEN/NP} - (E_{NP} + E_{GEN}) \quad ...(1)$$

Using the calculated binding energies of GEN/NP1-GEN/NP3 in Table 1, these energies are negative in solution phase indicating gentamicin is stabilized by γ-$Fe_2O_3$ nanoparticles surface. Among the 3 configurations in the solution phase, the configuration 2, in which the drug interacts with γ-$Fe_2O_3$ nanoparticles through hyroxyl (GEN/NP2) group, is the most stable configuration.

In describing stability and chemical reactivity of different systems, quantum molecular descriptors have been used like the chemical potential, the global hardness, the electrophilicity index and etc.

The chemical potential (μ) which shows escape tendency of an electron from equilibrium, is defined as follows:

$$\mu = -(I + A)/2 \quad ...(2)$$

where I=-$E_{HOMO}$ is the ionization potential and A-$E_{LUMO}$ is the electron affinity of the molecule. The global hardness (η) shows the resistance of one chemical species against the change in its electronic structure (Equation (3)). Increase in causes an increase in the stability and a decrease in reactivity.

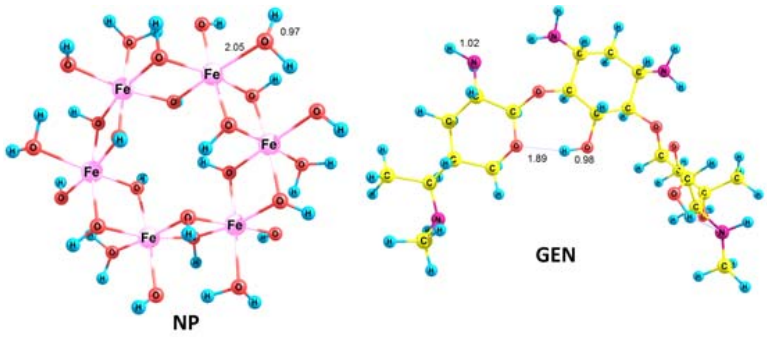



**Fig. 1: Optimized structure of $Fe_6(OH)_{18}(H_2O)_6$ or γ-$Fe_2O_3$ nanoparticle (NP) and gentamicin (GEN)**

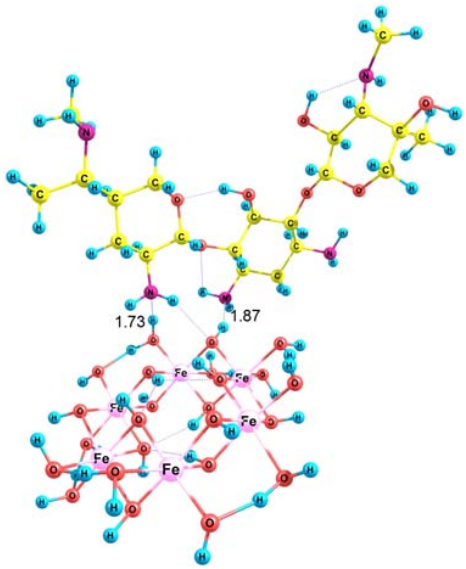



**Fig. 2: Optimized structure of GEN/NP1**

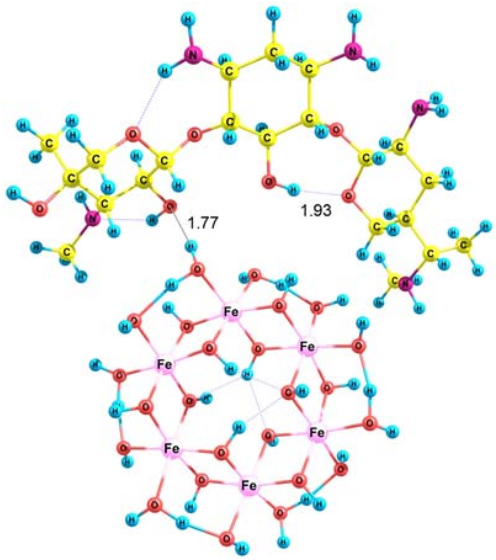



**Fig. 3: Optimized structure of GEN/NP2**

$$\eta = (I - A)/2 \quad ...(3)$$

Electrophilicity index (ω) was defined by Parr as follows[17]:

$$\omega = \mu^2 / 2\eta \quad ...(4)$$

Tabels 1 represents the values of the quantum molecular descriptors calculated for GEN, NP and GEN/NP1-3 in solution phases. In this table, besides quantum molecular descriptors, $E_g$ (HOMO-LUMO energy gap) was also presented. $E_g$ notably shows a more stable system.

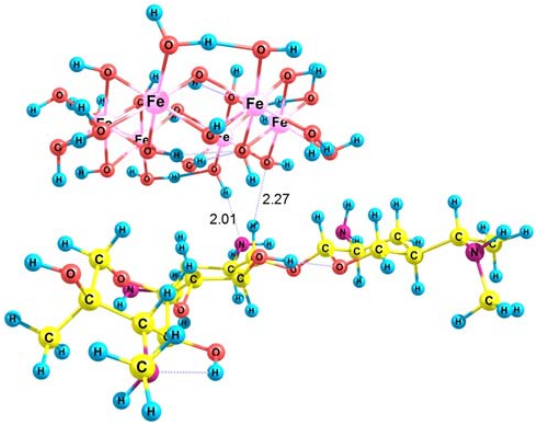



**Fig. 4. Optimized structure of GEN/NP3.**

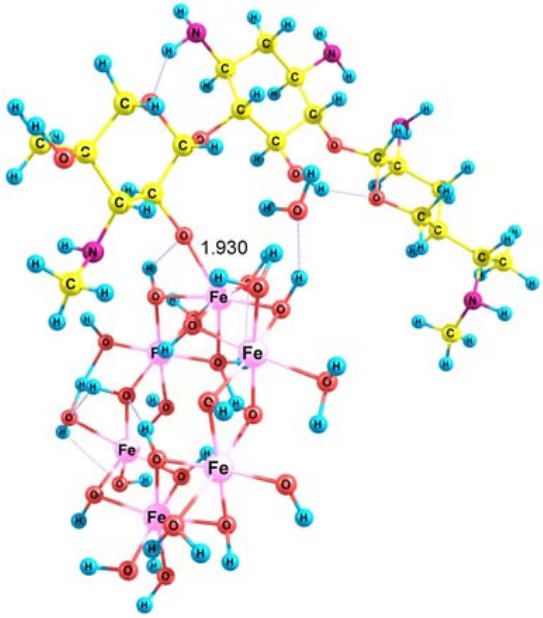



**Fig. 5: Optimized structure of GEN/NPC**

According to the data in Table 1, η, I, and $E_g$ related to the gentamicin drug are higher than GEN/NP1-3, showing the stability of the gentamicin decreases in the presence of γ-$Fe_2O_3$ nanoparticles and its reactivity increases. Also, in confirmation of the previous issue, it is observed that μ of the gentamicin becomes more negative in the presence of γ-$Fe_2O_3$ nanoparticles. ω of the gentamicin increases in the presence of γ-$Fe_2O_3$ nanoparticles, showing that the gentamicin acts as electron acceptor.

Six $H_2O$ molecules, due to weaker bond relative to OH, are proper choices which leave the cluster and are replaced by gentamicin. Scheme 1 shows the mechanism of covalent adsorption of GEN onto γ-$Fe_2O_3$ nanoparticles where $K_1$ and $K'_1$ are equilibrium constants and $k_1$ is rate constant (using GEN/NP2 as reactant).

species GEN/NP2 is initially formed with equilibrium constant $K_1$, following which the species GEN/NPC and product are formed in $k_1$ and $K'_1$ paths. The optimized structures of GEN/NPC has been shown in Fig. 5 (covalent adsorption). GEN/NPC is more stable than GEN/NP2 by 49.31 kJ/mol, so GEN/NPC is thermodynamic product.

## CONCLUSION

Using density functional theory, the effects of the adsorption of gentamicin onto γ-$Fe_2O_3$ nanoparticles have been studied in detail in solvent environment. Three possible modes of noncovalent interaction of Gentamicin onto γ-$Fe_2O_3$ nanoparticles were investigated. Besides parallel interaction (GEN/NP3), there are two possibilities for the formation of hydrogen bonds between gentamicin and ã-$Fe_2O_3$ nanoparticles, for the first possibility, gentamicin is interacted with γ-$Fe_2O_3$ nanoparticles through amino groups (GEN/NP1) and for the second one through hydroxyl groups (GEN/NP2). The product of second possibility is more stable.

## ACKNOWLEDGMENTS

We thank the theoretical research group in research center for animal development applied biology for allocation of computer time.

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