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DFT Study on the Adsorption of Drug 2-methoxyestradiol onto γ-Fe_2O_3 nanoparticles

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ABSTRACT

In this work, using quantum mechanics, the interaction of drug 2-methoxyestradiol with γ-Fe_2O_3 nanoparticles have been studied. Fe_2O_3 nanoparticles were modeled using $Fe_6(OH)_{18}(H2O)_6$ ring clusters. 2-methoxyestradiol molecule can coordinate to the γ-Fe_2O_3 nanoparticles via its own OH groups. All of the calculations have been performed using a hybrid density functional method (B3LYP) in solution phase. Two possible modes of noncovalent interaction of 2-methoxyestradiol onto γ-Fe_2O_3nanoparticles were investigated. Quantum molecular descriptors in the drug-nanoparticle systems were studied. It was found that binding of 2-methoxyestradiol with γ-Fe_2O_3nanoparticles is thermodynamically favorable. Therefore, γ-Fe_2O_3nanoparticlescanact as a suitable system for drug 2-methoxyestradiol delivery within biological systems.

Key words:2-methoxyestradiol, γ-Fe_2O_3nanoparticles, DFT, Drug delivery, Quantum molecular descriptors

INTRODUCTION

2-methoxyestradiol is an Antiangiogenesis agent which inhibits the growth of cancer cells such as leukemia, multiple myeloma, cervical, hepatocellular, colorectal, gastric, angiosarcoma, pancreatic and neuroblastoma[1-5].

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[6-9].

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[10]. 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 2-methoxyestradiol onto γ-Fe_2O_3 nanoparticles was studied.

MATERIALS AND METHODS

All of the present calculations have been performed with the B3LYP[11-13] hybrid density functional level using the GAUSSIAN 03 package[14]. 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[15-19]. The implicit effects of the solvent was considered by using the polarized continuum model (PCM)[20]. 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 2-methoxyestradiol (MET), $Fe_6(OH)_{18}(H_2O)_6$ or γ-Fe_2O_3 nanoparticle (NP) in solution phase are shown in Fig. 1. 2-methoxyestradiol is a non-planar molecule with the hydroxyl groups protruding out of the molecular plane as shown in Fig. 1.

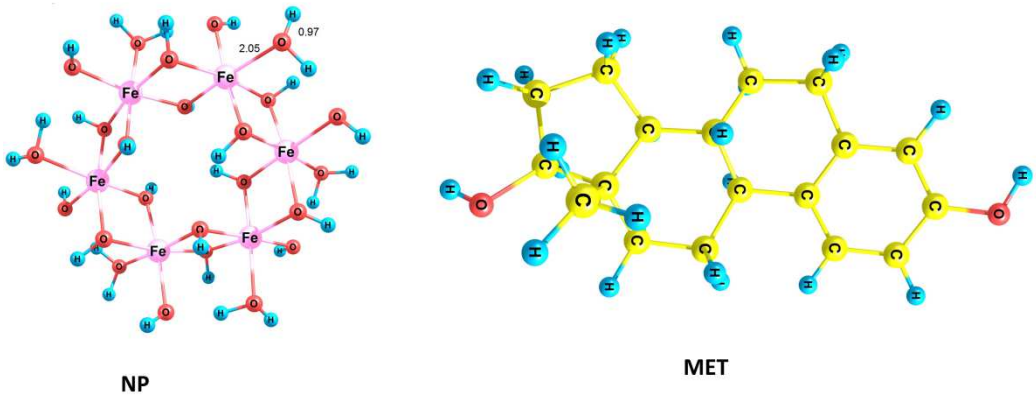

Fig. 1. Optimized structure of $Fe_6(OH)_{18}(H_2O)_6$ or γ-Fe_2O_3 nanoparticle (NP) and 2-methoxyestradiol (MET)

Two possible modes of noncovalent interaction of 2-methoxyestradiol onto γ-Fe_2O_3 nanoparticles were studied. Figures 2 and 3 present these configurations in solution phase, namely, NP/MET1 and NP/MET2. 2-methoxyestradiol may interact with γ-Fe_2O_3 nanoparticles through hyroxyl (NP/MET1-2) groups to form hydrogen bonds.

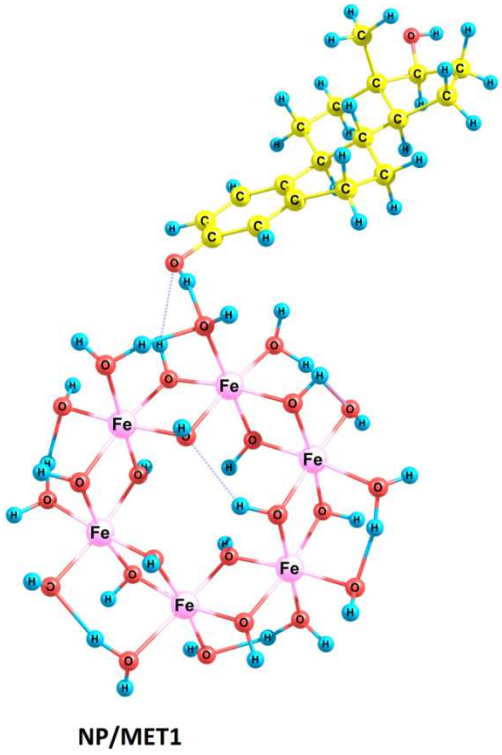

Fig. 2. Optimized structure of NP/MET1

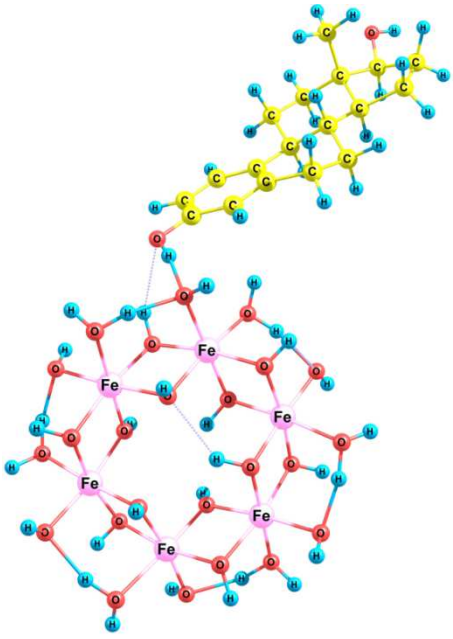

Fig. 3. Optimized structure of NP/MET2

The binding energies (E_b) of 2-methoxyestradiol whit γ-Fe_2O_3 nanoparticles are calculated using the following equation and presented in Table 1:

$$E_b = E_{NP/MET} - (E_{NP} + E_{GEN}) \qquad (1)$$

Using the calculated binding energies of NP/MET1- NP/MET2 in Table 1, these energies are negative in solution phase indicating 2-methoxyestradiol is stabilized by γ-Fe_2O_3 nanoparticlessurface. Among the 2 configurations in the solution phase, the configuration NP/MET1, in which the drug interacts with γ-Fe_2O_3 nanoparticles through hyroxyl (NP/MET1) group, is the most stable configuration.

In describing stability and chemical reactivity of different systems, quantum molecular descriptorshave 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:

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

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 η causes an increase in the stability and a decrease in reactivity.

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

Electrophilicity index (ω) was defined by Parr as follows[21]:

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

Table 1 represents the values of the quantum molecular descriptors calculated for MET, NP and NP/MET1-2 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.

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

Species	E_b	E_{HOMO}	E_{LUMO}	E_g	η	μ	ω	E(Hartree)
MET	-	-5,63	0,10	5,73	2,86	-2,77	1,34	-850.86900
NP	-	-5,58	-4,48	1,10	0,55	-5,03	23,00	-2564.50735
NP/MET1	-13.65	-5,63	-4,56	1,07	0,54	-5,10	24,26	-3415.38156
NP/MET2	-12.39	-5,60	-4,48	1,12	0,56	-5,04	22,68	-3415.38108

According to the data in Table 1, η, I, and E_g related to the 2-methoxyestradiol drug are higher than NP/MET 1-2, showing the stability of the 2-methoxyestradiol 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 2-methoxyestradiol becomes more negative in the presence of γ-Fe_2O_3 nanoparticles. ω of the 2-methoxyestradiol increases in the presence of γ-Fe_2O_3 nanoparticles, showing that the 2-methoxyestradiol acts as electron acceptor.

CONCLUSION

Using density functional theory, the effects of the adsorption of 2-methoxyestradiol onto γ-Fe_2O_3 nanoparticles have been studied in detail in solvent environment. Two possible modes of noncovalent interaction of 2-methoxyestradiol onto γ-Fe_2O_3 nanoparticles were investigated. There are two possibilities for the formation of hydrogen bonds between 2-methoxyestradioland γ-Fe_2O_3nanoparticles, for the first possibility, 2-methoxyestradiol is interacted with γ-Fe_2O_3 nanoparticles through OH1 groups (NP/MET1) and for the second one through OH2 (NP/MET2). Calculations show the stability of the 2-methoxyestradiol decreases in the presence of γ-Fe_2O_3 nanoparticles and its reactivity increases.

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