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Research Article

THEORETICAL STUDY ON PHYSICOCHEMICAL AND GEOMETRICAL PROPERTIES OF THE ADRIAMYCIN CONJUGATED GOLD NANOPARTICLES

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ABSTRACT

Adriamycin (or Doxorubicin) is well known anti-cancer agent. It is an anthracycline antibiotic. The use of Adriamycin against neoplasms is limited due to its severe cardiotoxicity. The cytotoxicity of Adriamycin can be minimized by linking it to an affinity tag. In this report, the molecular structure, Binding Energy (BE), Dipole Moment (DM), log P and some physicochemical properties of Adriamycin and Adriamycin conjugated gold nanoparticles were investigated using Density functional Theory (DFT) calculations. Our results indicate that this complex mentioned above can be used to improve anti cancer activity and water-solubility of Adriamycin.

Keywords: Anti-cancer drug, DFT calculations, Adriamycin-gold nanoparticles, Adriamycin.

INTRODUCTION

One of the most ordinary used anticancer medicines is Adriamycin. It is an anthracycline antibiotic, which intercalates DNA. Adriamycin is used to medicate a vast range of cancers, including hematological malignancies, many types of carcinoma, and soft tissue sarcomas. Nevertheless, when Adriamycin is applied directly, it is without the tumor-targeting ability leading to poor bio-distribution and curative effects as well as critical unpleasant side effects. The scheme of Adriamycin is illustrated in Fig 1.

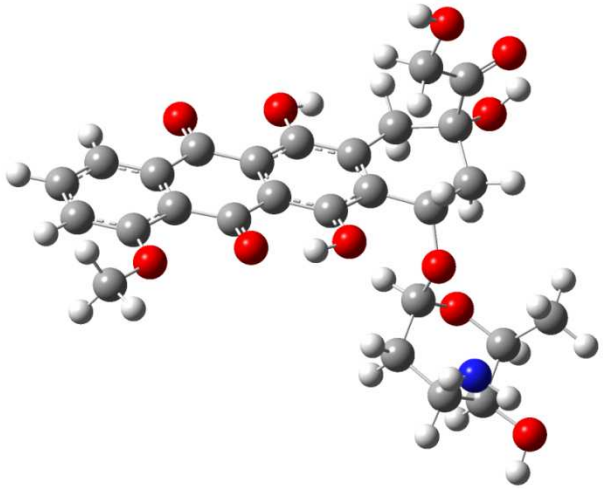

Fig. 1: the Structure optimized Adriamycin

In empirical studies conducted by some other researchers, it has been clarified that Gold nanoparticles (Au NPs) have been the matter of intense investigation throughout the past decade because of their possible use in drug delivery, sensing, imaging and chemotherapy1-6. Au NPs have distinguishing features, for example, their sizes can be simply conducted during combination and their surfaces can be easily functionalized with different kinds of molecules7-10. Properly functionalized Au NPs not only can act as a drug reservoir, but also supply a long circulation time and cytotoxicity, so, they have appeared as attractive candidates for distributing different payloads into their targets10-12. The payloads could be small medicine molecules or large biomolecules such as proteins, DNA or RNA.

Effective freeing of these therapeutic elements at the target place is essential for efficient therapy. Payloads release can be activate by internal (e.g., glutathione (GSH) or pH) or external (e.g., light) stimuli[13-15]. Furthermore, drug delivery systems (DDSs) with a high drug loading level can act as 'drug reservoirs' for supplied and supported drug release, thereby protecting the drug application within the therapeutic window. There have been a number of interesting statements in recent years on the use of functionalized Au NPs for drug delivery usage. Gibson et al. announced the direct functionalization of Au NPs with paclitaxel using hexaethylene glycol as a connection for cancer therapy[16]. Tom et al. investigate the drug release manner of ciprofloxacin functionalized Au NPs and discovered that it was influenced by both the size of the functionalized Au NPs and the type of release medium[17]. Paciotti et al. functionalized Au NPs with a combination of tumor necrosis component (TNC), PEG and paclitaxel, which was worked as a multifunctional vector susceptible to target solid tumors[10,12]. Because Au NPs can begin local heating when they are illuminated with light, ElSayed et al. investigate the possible usage of Au NPs in photothermal demolition of tumor tissues. In their researches, citrate-stabilized Au NPs were covered with an anti-epidermal increase element receptor (EIER) to target human oral squamous cell carcinoma (HSC3 cancer cells)[18,19]. In another research, Paasonen et al. Created an optically reactive delivery system by merging Au NPs into liposomes Upon UV exposure, fluorescent markers contained in the liposomes were release, which was expedited by the heating of the Au NPs[20]. In comparison with polymeric micelles and liposomes, which are extensively research for hydrophobic drug delivery usage, functionalized Au NPs usually have much smaller sizes that are preferable for (1) inactive targeting of tumor tissues via the increased permeation and retention (IPR) effect; and (2) decreased reticuloendothelial system (IES) clearance[21-23].

Many studies indicated and confirmed that coating nanoparticles with PEG car decrease opsonization on their surface and extend the circulation time in the blood stream, thereby let the nanoparticles to reach the tumor tissue via the EPR[4].

Adriamycin conjugated gold nanoparticles complex was synthesized by Shaoqin Gong and colleagues[24]. The conjugation scheme is in Fig. 2. Furthermore, the optimized structure of Adriamycin conjugated Au NPs has been showed in Fig. 3. The geometry of Adriamycin conjugated Au NPs were optimized at B3LYP/6-31g* level of theory using Gaussian 03[25]. In study unit number of PEG is 2.

In this study Quantum mechanical molecular simulation can be used to study drug delivery.

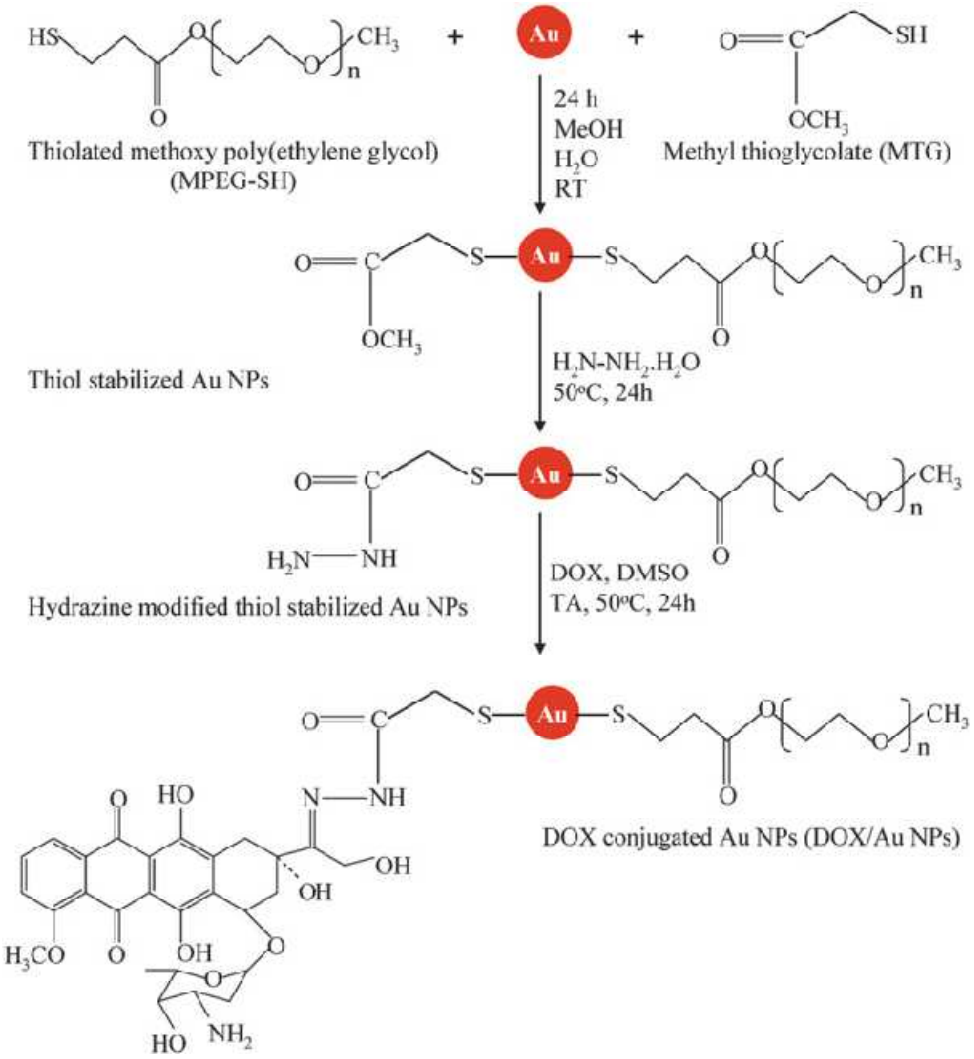

Fig. 2: Synthesis scheme for the preparation of Adriamycin conjugated Au NPs[24].

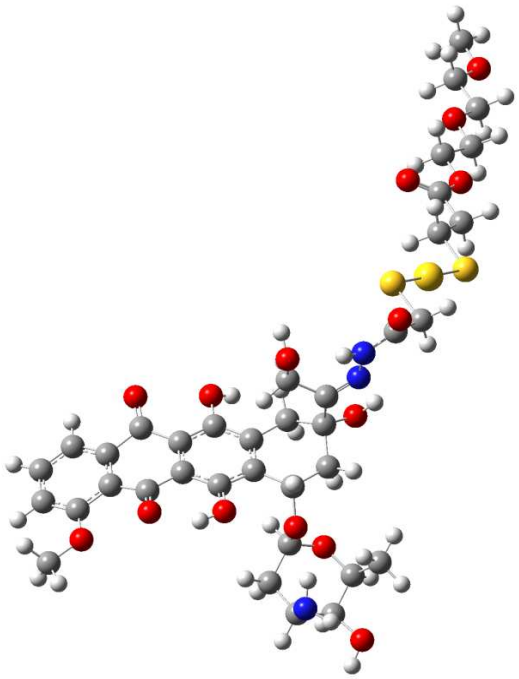

Fig. 3: Structure optimized of Adriamycin conjugated Au NPs n=2

In this study, we intend to show some the characteristics of Adriamycin, Adriamycin conjugated Au NPs which have been mentioned above and have been obtained by other researchers experimentally through predictable computational calculations including molecular energy, binding energy, dipole moment, log P, distance bound and angle bound[26].

RESULTS AND DISCUSSION

The geometry structure of Adriamycin and Adriamycin conjugated Au NPs were optimized at B3LYP/6-31g* level of theory. Table 1 presents the geometrical parameters of this complex mentioned above around linking position (hydrazon group), see also Fig 4.

Some physicochemical properties of Adriamycin conjugated Au NPs and Adriamycin such as Refrectivity, polarizability, Hydration energy, binding energies (BE), log P and Dipole moment (DM) are obtained from optimal structure[27] which have been shown in Table 2. The binding energy per molecule was computed using the formula (1):

$$\Delta E = E_{complex} - E_{drug} - E_{carrier} \quad (1)$$

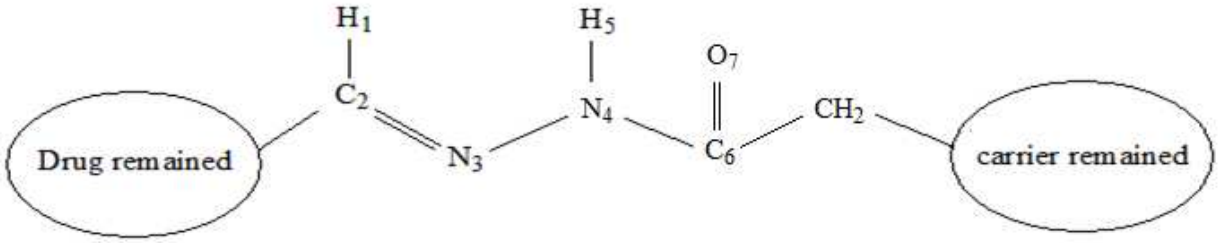

Fig. 4: Structure of linking position in Adriamycin conjugated Au NPs complex.

Table 1: Geometrical parameter of complex around linking position

Complex	R(C_1=N_2) (Å)	R(N_2=N_3) (Å)	R(N_3-C_5) (Å)	C_1-N_2-N_3 (°)	N_3-C_5-O_6 (°)
Adriamycin conjugated Au NPs	1.297	1.391	1.377	111.877	119.881

Table 2: Some calculated physicochemical properties of Adriamycin conjugated Au NPs and Adriamycin

Physicochemical properties	Adriamycin-Au NPs	Adriamycin
Refrectivity[a]	206.06	135.50
Polarizability	81.41	52.00
Hydration energy[a]	-31.27	-24.03
Surface area[a](Å2)	1138.88	729.45
Log P[a]	-0.03	0.03
Dipole moment(Debye)	7.025	6.848
BE (ev/mol)	-1069.919	-

[a]Data were calculated using HyperChem 8 software[28]

CONCLUSION

Density functional Theory (DFT) calculations were applied to study some physicochemical properties of Adriamycin conjugated Au NPs and Adriamycin.

Regarding the calculation results, hydrophilicity of Adriamycin conjugated Au NPs is higher than that of Adriamycin; this fact can be verified through the logP obtained for this complex using Hyperchem. therefore, Adriamycin conjugated Au NPs is more soluble than of Adriamycin. These calculations also show that Adriamycin release from Adriamycin conjugated Au NPs complex takes place in a long period of time. On the other hand it means that we have a gradual release which is predictable according to Binding Energy.

Our results indicate that this complex mentioned above can be used to improve anti cancer activity and water-solubility of Adriamycin.

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