Available online at www.sciencedirect.com

ScienceDirect

Procedia Materials Science 11 (2015) 131 – 136

Procedia Materials Science

www.elsevier.com/locate/procedia

5th International Biennial Conference on Ultrafine Grained and Nanostructured Materials, UFGNSM15

Carbon Nanotubes for Delivery of Quercetin as Anticancer Drug: Theoretical Study

S. Daneshmehr[a,*]

[a]*Young Researchers and Elite Club, Tabriz Branch, Islamic Azad University, Tabriz, Iran*

Abstract

Single walled carbon nanotubes as free-radical scavengers and novel drug carriers are important in the drug delivery systems because of their high selectivity to target for cancer cells. Quercetin, one of Flavonoids derivatives, has effective chemopreventive and anticancer properties. This study was done to investigate the effect of configuration between SWCNT (5,5) and Quercetin at gas phase and polarizable continuum model (PCM). Calculations have been done at the DFT level with using of hybrid density functional (B3LYP) and 6-31G (d,p) basis set. Results showed that the gas phase or PCM had no significant effect on CNT beside Quercetin as drug delivery systems.

Peer-review under responsibility of the organizing committee of UFGNSM15

Keywords: Quercetin; Anticancer; DFT; CNT; Drug.

1. Introduction

A group of polyphenolic compounds widely found in the medicinal plants, vegetables, fruit juices and a variety of beverages are flavonoids, Moo-Huchin et al. (2015), Sieliwoniuk et al. (2015). Flavonoids, mainly quercetin derivatives, are considered as dietary constituents and they have a significant role in human health, including cardiovascular protection, anticancer activity, antiulcer effects, antiallergic, antiviral, and anti-inflammatory properties, Hussain et al. (2015). Quercetin, whose anticancer properties have been verified in vivo and in vitro experiments, is one of the natural antioxidants, Russo et al. (2014). Studies indicated that quercetin has beneficial

* Corresponding author. Tel.:: +984133396085; fax: +984133320192.
E-mail address: shahladaneshmehr@yahoo.com

Peer-review under responsibility of the organizing committee of UFGNSM15
doi:10.1016/j.mspro.2015.11.128

effects on inhibition of breast, colon, prostate, ovary, endometrium, and lung tumor cancer cells. Also quercetin is used as ions chelating agent and it prevents reactions between DNA and ions, Jakhar et al. (2014), Li et al. (2014). Quercetin is widely distributed in main food resources such as fruits and vegetables especially citrus, apple, onion, parsley, green tea, olive oil, grape, cherry, black mulberry, dogberry, and raspberry, Bukhari et al. (2008). Scientists have investigated new controlled drug delivery systems in order to get different achievement, including: delivery of therapeutic agents to the desired site, enhancing bioavailability and drug protection, Doane and Burda (2012), Kumara and Mohammad (2011), Peppas and Blanchette (2004). These investigations caused nanomedicine a new emerging field includes the application of nanotechnology in medicine. It has potential to develop area of therapeutic delivery Amiji (2006), Kayser et al. (2005). A group of new nanoscale materials including: nanoparticles, nanotubes, nanofibers, dendrimers, liposomes, polymer micelles, nanogels, nanocrystals, viral vectors, and virus-like particles have been studied for drug delivery applications in recent years Amiji (2006), Hughes (2005), Regi et al. (2007), Wei et al. (2007). In these materials, CNTs that has unique chemical and physical properties has been considered more in drug delivery applications Meng et al. (2012), Biju (2014). CNTs can be used in cancer therapy and other areas of medicine as a drug-delivery vehicles or nanocarriers without damaging the healthy tissues, Kesharwani et al. (2014), Prakash et al. (2011). The polymeric part (polymethacrylic acid, PMAA) increases the flavonoid water solubility and enhances its stability in order to have a sustained activity over time, Cirillo et al. (2013), López-De-Dicastillo et al. (2012), Leonarduzzi et al. (2010). Today these nanotubes are used to deliver cancerous and non-cancerous drugs to different cells in vitro and in vivo and it is hoped that they would be used in gene therapy, vaccination, and different cancer treatments in the future, Mura et al. (2013), Fabbro et al. (2012). Because theoretical study of the interaction between SWCNTs and Quercetin has not been done yet our main objective in the present study is to investigate theoretically the interaction of SWCNTs beside Quercetin with four types of different configuration including covalent and noncovalent bindings. We hope the results presented could lead to better condition for the usage of nanostructures in assisting Quercetin as drug carriers.

2. Computational details

All the calculations have been done at the DFT level with using of hybrid density functional (B3LYP) and 6-31G (d,p) basis set at gas phase and polarizable continuum model (PCM). The zero point energies (ΔZPE), electronic energies (ΔE), enthalpies (ΔH) and free Gibbs energies (ΔG) were calculated using the following equation, Veloso et al. (2006):

$$\Delta E\ (state\ x) = E_{state\ X} - E_{CNTCOOH} - E_{Q}$$

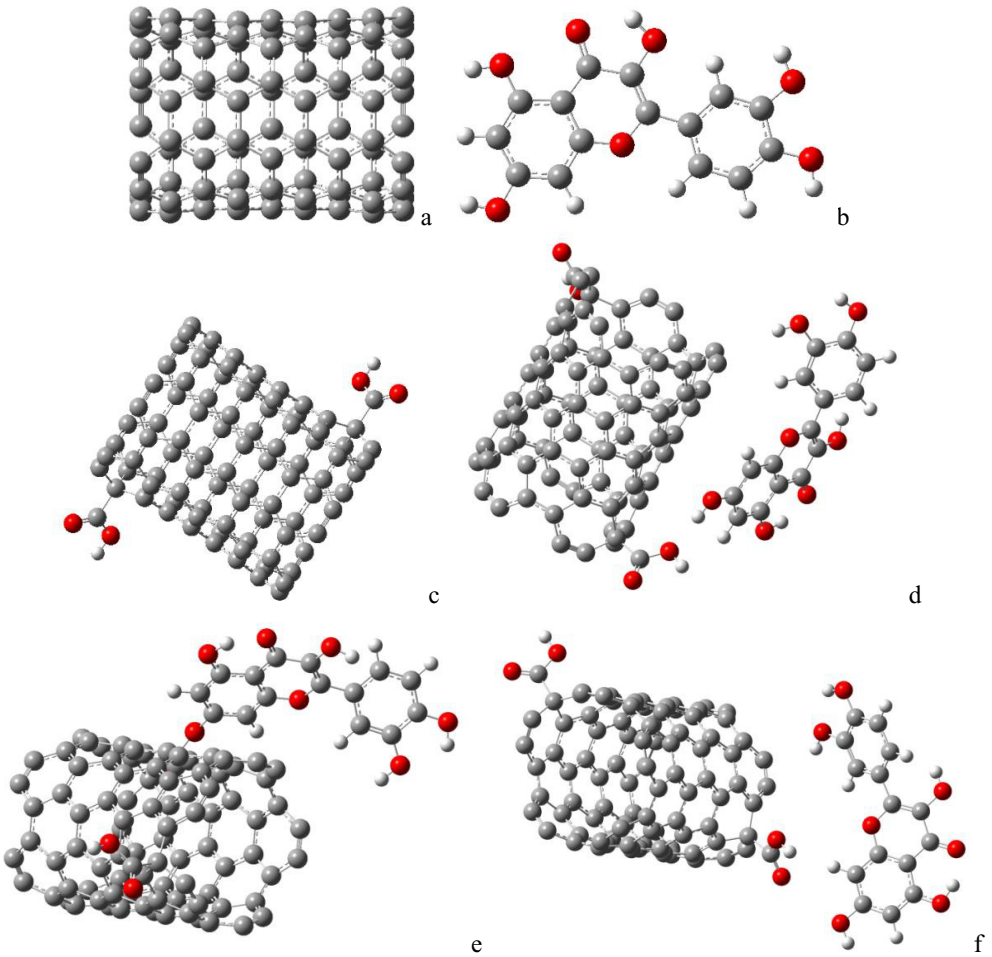
where $E_{state\ X}$ is the total energy of the nanotube and MAA with the attached Quercetin, $E_{CNTCOOH}$ is the electronic energy of the CNT and MAA (CNTCOOH), and E_Q is the electronic energy of the Quercetin. All calculations were performed using the GAUSSIAN 03 program, Frisch et al. (2004).

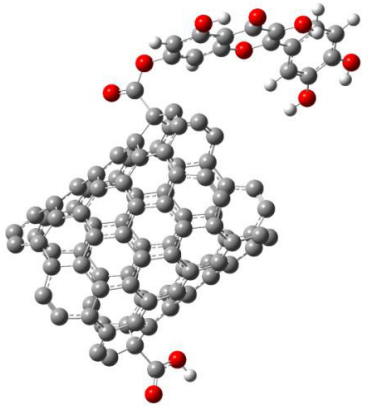
3. Results and Discussion

Figure 1 shows the graphical representations of the optimized geometries carbon nanotube (5,5), carbon nanotube/MAA and carbon nanotube/MAA beside Quercetin at four differences configurations including covalent and noncovalent bindings. Table 1 and 2 display the values of the zero-point energies (ZPE), electronic energies, enthalpies and Gibbs free energy for CNT, CNTCOOH and CNTCOOH/Q at different states using B3LYP with 6-31G (d,p) basis sets at gas phase and polarizable continuum model (PCM), respectively. Table 3 and 4 display the calculated relative energies (ΔE), enthalpies (ΔH) and free Gibbs energies (ΔG) in gas phase and PCM, for CNT beside Quercetin at the room temperature. From Table 3 and 4, it can be seen that state 3 has less values of relative energies (ΔE), enthalpies (ΔH) and free Gibbs energies (ΔG) than three other states in gas phase and PCM.

Table 1. Theoretical data at gas phase.

	ZPE(kJ/mol)	Energies(kJ/mol)	Enthalpies(kJ/mol)	Gibbs Free Energy(kJ/mol)
CNTCOOH gas	-3806.186782	-3806.135284	-3806.134340	-3806.259373
Quercetic gas	-1104.260823	-1104.242157	-1104.241213	-1104.307578
State 1	-4908. 615314	-4908.194513	-4908.233194	-4908.269507
State 2	-4909.054267	-4908.95782	-4908.875214	-4908.965024
State 3	-4910.165615	-4910.094093	-4910.093149	-4910.268031
State 4	-4909.151456	-4909.15704	-4909.162347	-4909.162354





g

Fig. 1. Optimized geometrical parameters of (a) CNT (5,5), b) MAA; (c) CNT/MAA; (d) State 1; (e) State 2; (f) State 3; (g) State 4 at gas phase and PCM.

Table 2. Theoretical data at polarizable continuum model (PCM).

	ZPE(kJ/mol)	Energies(kJ/mol)	Enthalpies(kJ/mol)	Gibbs Free Energy(kJ/mol)
CNTCOOH gas	-3806.204288	-3806.152475	-3806.151531	-3806.277063
Quercetic gas	-1103.980293	-1103.962846	-1103.961901	-1104.024678
State 1	-4909.196135	-4909.124150	-4909.123206	-4909.296208
State 2	-4908.947821	-4908. 646985	-4908.939071	-4908.067654
State 3	-4909.541961	-4909.742876	-4909.986597	-4909.024978
State 4	-4908.767924	-4908.698645	-4908.697701	-4808.863920

Table 3. Calculated relative electronic energies (kJ/mol), enthalpies (kJ/mol) and free Gibbs energies (kJ/mol) in gas phase.

	ZPE(kJ/mol)	Energies(kJ/mol)	Enthalpies(kJ/mol)	Gibbs Free Energy(kJ/mol)
State 1	4721.31	5725.71	5613.11	6032.78
State 2	2189.34	3730.30	3935.31	3698.30
State 3	745.93	749.92	739.28	280.54
State 4	3406.01	3207.76	3180.73	3180.71

Table 4. Calculated relative electronic energies (kJ/mol), enthalpies (kJ/mol) and free Gibbs energies (kJ/mol) in PCM.

	ZPE(kJ/mol)	Energies(kJ/mol)	Enthalpies(kJ/mol)	Gibbs Free Energy(kJ/mol)
State 1	2592.432	2598.95	2598.803	2635.519
State 2	3243.747	3868.851	3081.78	5857.955
State 3	1685.348	976.0626	334.1717	3346.942
State 4	3715.608	3715.028	3714.881	266064.4

4. Conclusion

Comparison studies of DFT calculations at B3LYP with 6-31G (d,p) basis set at gas phase and PCM for CNT and MAA beside Quercetin in order to find the best configuration at drug delivery system were done. Results indicated that different configurations had no significant effects at gas phase and PCM and state 3 was the best nanocarrier among other states.

References

.Li, X., Zheng, T., Sang, S., Lv, L., 2014. Quercetin inhibits advanced glycation end product formation by trapping methylglyoxal and glyoxal. Journal of Agricultural and Food Chemistry 62(50), 12152-12158.

Amiji, M.M., 2006. Nanotechnology for targeted drug and gene delivery. Nanomedicine 2, 299-300.

Biju, V., 2014. Chemical modifications and bioconjugate reactions of nanomaterials for sensing, imaging, drug delivery and therapy. Chemical Society Reviews 43, 744-764.

Bukhari, S.B., Memon, S., Tahir, M.M., Bhanger, M.I., 2008. Synthesis, characterization and investigation of antioxidant activity of cobalt–quercetin complex. Journal of Molecular Structure 892(1-3), 39-46.

Cirillo, G., Vittorio, O., Hampel, S., Iemma, F., Parchi, P., Cecchini, M., Puoci, F., Picci, N., 2013. Quercetin nanocomposite as novel anticancer therapeutic: improved efficiency and reduced toxicity. European Journal of Pharmaceutical Sciences 49, 359-365.

Doane, T.L., Burda, C., 2012. The unique role of nanoparticles in nanomedicine: imaging, drug delivery and therapy. Chemical Society Reviews 41, 2885-2911.

Fabbro, C., Ali-Boucetta, H., Da Ros, T., Kostarelos, K., Bianco, A., Prato, M., 2012. Targeting carbon nanotubes against cancer. Chemical Communications 48, 3911-3926.

Hughes, G.A., 2005. Nanostructure-mediated drug delivery. Nanomedicine 1, 22-30.

Hussain, S.A., Panjagari, N.R., Singh, R.R.B., Patil, G.R., 2015. Potential herbs and herbal nutraceuticals: food applications and their interactions with food components. Critical Reviews in Food Science and Nutrition 55, 94-122.

Jakhar, R., Paul, S., Park, Y.R., Han, J., Kang, S.C., 2014. Pentamethoxyflavone, a quercetin derivative protects DNA from oxidative challenges: Potential mechanism of action. Journal of Photochemistry and Photobiology B-Biology 131, 96-103.

Kayser, O., Lemke, A., Trejo, N.H., 2005. The impact of nano biotechnology on the development of new drug delivery systems. Current Pharmaceutical Biotechnology 6, 3-5.

Kesharwani, P., Jain, K., Jain, N.K., 2014. Dendrimer as nanocarrier for drug delivery. Progress in Polymer Science 39(2), 268-307.

Kumara, C.S.S.R., Mohammad, F., 2011. Magnetic nanomaterials for hyperthermia-based therapy and controlled drug delivery. Advanced Drug Delivery Reviews 63(9), 789-808.

Leonarduzzi, G., Testa, G., Sottero, G.S., Gamba, P., Poli, G., 2010. Design and development of nanovehicle-based delivery systems for preventive or therapeutic supplementation with flavonoids. Current Medicinal Chemistry 17, 74-95.

López-De-Dicastillo, C., Alonso, J.M., Catalá, R., Gavara, R., Hernández-Munoz, P., 2012. Improving the antioxidant protection of packaged food by incorporating natural flavonoids into ethylene-vinyl alcohol copolymer (EVOH) films. Journal of Agricultural and Food Chemistry 58, 10958-10964.

Meng, L., Zhang, X., Lu, Q., Fei, Z., Dyson, P.J., 2012. Single walled carbon nanotubes as drug delivery vehicles: targeting doxorubicin to tumors. Biomaterials 33, 1689-1698.

Moo-Huchin, V.M., Moo-Huchin, M.I., Estrada-León, R.J., Cuevas-Glory, L., Estrada-Mota, I.A., Ortiz-Vázquez, E., Betancur-Ancona, D., Sauri-Duch, E., 2015. Antioxidant compounds, antioxidant activity and phenolic content in peel from three tropical fruits from Yucatan, Mexico. Food Chemistry 166, 17-22.

Mura, S., Nicolas, J., Couvreur, P., 2013. Stimuli-responsive nanocarriers for drug delivery. Nature Materials 12, 991-1003.

Peppas, L.B., Blanchette, J.O., 2004. Nanoparticle and targeted systems for cancer therapy. Advanced Drug Delivery Reviews 56, 1649-1659.

Prakash, S., Malhotra, M., Shao, W., Duchesneau, C.T., Abbasi, S., 2011. Polymeric nanohybrids and functionalized carbon nanotubes as drug delivery carriers for cancer therapy. Advanced Drug Delivery Reviews 63(14–15), 1340-1351.

Regi, M.V., Balas, F., Arcos, D., 2007. Mesoporous materials for drug delivery. Angewandte Chemie-International Edition 46, 7548-7558.

Russo, G.L., Russo, M., Castellano, I., Napolitano, A., Palumbo, A., 2014. Ovothiol isolated from sea urchin oocytes induces autophagy in the hep-g2 cell line. Marine Drugs 12(7), 4069-4085.

Sieliwoniuk, E.N., Malejko, J., Swieczkowska, M., Kowalewska, A., 2015. A study on the selection of chemiluminescence system for the flow injection determination of the total polyphenol index of plant-derived foods. Food Chemistry 176, 175-183.

Veloso, M.V., Souza Filho, A.G., Mendes Filho, J., Fagan, S.B., Mota, R., 2006. Ab initio study of covalently functionalized carbon nanotubes. Chemical Physics Letters 430, 71.

Wei, C., Wei, W., Morris, M., Kondo, E., Gorbounov, M., Tomalia, D.A., 2007. Nanomedicine and drug delivery. Medical Clinics of North America 91, 863-870.