Possibility of using fullerene C_{240} as the carrier of steroid hormones

Fullerene molecules are created entirely of carbon and form orbicular or ellipsoidal cage shape similar to a hollow tube. The derivatives of fullerenes are classified into the following categories according to their functionalization: endohedral fullerenes with active molecules residing inside the carbon cage, exohedral with wide variety of both inorganic and organic groups existing outside and connected to the fullerenes' exterior and heterofullerenes when one or more carbon atoms that form the fullerene carbon cage are replaced by a non-carbon atom, i.e. a heteroatom. Fullerene C_{240}belongs to the family of giant fullerenes and is characterized by a greater stability than that of the well-known fullerene C_{60}. This has been proved by observing an increased formation heat that accompanied the decreasing of the carbon cage size.In order to determine the fullerene C_{240} ability to transport the steroid hormones: estradiol, progesterone, androsterone and their basic structures: estrone, androstane and pregnane, the following parameters, inter alia, have been calculated: energies of stabilization, interaction and deformation of each endohedral complex. The calculations for all chosen structures were carried out with the use of the molecular modeling technique. Based on all available studies, it can be stated that fullerene C_{240} could be a solution for problems faced by medicine and pharmacy.

PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.1869v1 | CC-BY 4.0 Open Access | rec: 17 Mar 2016, publ: 17 Mar 2016

POSSIBILITY OF USING FULLERENE C_{240} AS THE CARRIER OF STEROID HORMONES

*Monika K. GRUDZIEŃ[1], Izabela WIŚNIEWSKA[1], Marcin SUSKIEWICZ[1], Tomasz PIEŃKO[1], Aleksander P. MAZUREK[1,2]

[1]*Department of Drug Chemistry, Faculty of Pharmacy with the Laboratory Medicine Division, Medical University of Warsaw, 1, Banacha str., 02-097 Warsaw, Poland*
[2] *Department of Basic and Applied Pharmacy, National Medicines Institute, 30/34, Chełmska str., 00-725 Warsaw, Poland*

**monika.grudzien@wum.edu.pl*

Fullerene molecules are created entirely of carbon and form orbicular or ellipsoidal cage shape similar to a hollow tube. The derivatives of fullerenes are classified into the following categories according to their functionalization:

- endohedral fullerenes with active molecules residing inside the carbon cage,
- exohedral with wide variety of both inorganic and organic groups existing outside and connected to the fullerenes' exterior,
- heterofullerenes when one or more carbon atoms that form the fullerene carbon cage are replaced by a non-carbon atom, i.e., a heteroatom.

The attributes of fullerenes, such as the structure, geometry, size and shape of the carbon cage, indicate the possibility of using them as vehicles for transporting the pharmacologically active substance into the target cell [1].

Fullerene C_{240} belongs to the family of giant fullerenes and is characterized by a greater stability than that of the well-known fullerene C_{60}. This has been proved by observing an increased formation heat that accompanied the decreasing of the carbon cage size. The lower formation heat guarantees the greater fullerene stability: C_{60} heat equals 40.02 kJ·mol^{-1} while C_{240} heat equals 23.95 kJ ·mol^{-1} [2].

Quantum-mechanical calculations show that icosahedral structures, which include the C_{240} fullerene, are the most enduring. These are objects with a strong surface curvature in areas where there are pentagonal and heptagonal rings. The flat fragments are hexagonal while the fullerene C_{240} viewed along the three axes of symmetry has a spheric shape when observed along its fivefold symmetry axis (C5) and the polyhedral figure when watched along the threefold axis (C3) [3].

The steroid hormones impact on many features and functions of the human organism such as body structure and biochemical or physiological processes. The estrogens are used for treating estrogen deficiency, osteoporosis, in alternative contraception and prostate cancer. Androgens are used in the absence of maturation, hypogonadism and male infertility. They are also used in treatment of endometriosis at women and as a palliative treatment of metastatic breast cancer [4,5].

In order to determine the fullerene C_{240} ability to transport the steroid hormones: estradiol, progesterone, androsterone and their basic structures: estrone, androstane and pregnane, the following parameters, inter alia, have been calculated: energies of stabilization, interaction and deformation of each endohedral complex, the optimization procedure influence on each compound, fullerene geometry and minimal distance structures enclosed in C_{240} cage from the carbon cage.

The calculations for all chosen structures were carried out with the use of the molecular modeling technique (HF, STO-3G base implemented in Spartan'14 software) [6]. The first calculation stage was geometry optimization, establishing the most stable conformation and the absolute energy (in energetic minimum) of each examined compound. After that, all the lowest energy conformers were placed into carbon cage of fullerene C_{240} and each complex geometry was optimized. The next step was delimitation of total energy of endohedral complexes. Finally, the energy values in geometry from endohedral complex - compound@C_{240} for estradiol, progesterone, androsterone, estrone, androstane, pregnane and empty carbon cage have been calculated. The last step was delimitation of energies: stabilization (ΔE_{stab}), interaction ($\Delta E_{int.}$) and deformation (ΔE_{def}). The results have been shown in Table 1. below.

Table 1. The energies calculated for all examined compounds.

Compound	ΔE_{stab} [kcal·mol^{-1}]	ΔE_{int} [kcal·mol^{-1}]	ΔE_{def}[kcal·mol^{-1}]
Estrone	21,21	12,91	8,28
Estradiol	- 56,64	19,36	- 77,77
Androstane	56,28	27,56	25,70
Androsterone	56,09	22,86	30,94
Pregnane	57,49	25,79	29,40
Progesterone	67,50	23,38	42,22

The endohedral fullerene complex is stable when the stabilization energy takes negative values. The higher is the value, the lower is stability of the formed complex. On the other hand, a positive value indicates instability of the complex.

The results show that the complexes formed by all structures, except estradiol, are thermodynamically unstable. The cause of instability of complexes may be the presence of the weak interaction between the fullerene and hormones or their model structures. These are mainly the interactions of Van der Waals type.

PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.1869v1 | CC-BY 4.0 Open Access | rec: 17 Mar 2016, publ: 17 Mar 2016

Only one compound formed a stable complex, namely estradiol. The calculated stabilization energy value for its endohedral complex estradiol@C_{240} is -56.64 kcal·mol^{-1}.

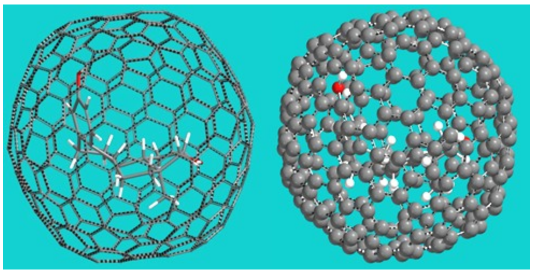

Fig 1. The stable complex estradiol@C_{240} [6].

Based on all available studies, it can be stated that fullerene C_{240} could be a solution for problems faced by medicine and pharmacy. It can be used as a transporter of steroid hormones. This is confirmed by the fact that none of the complex that carried out the optimization procedure has not been destroyed. Moreover, all optimized structures of “guests” trapped into “host” cage tried to occupy a place in the central part of fullerene C_{240}.

References:

[1] M.K. Grudzień, M. Suskiewicz, E. Ajmanovič, M. Mędrek, F.A. Pluciński, A.P. Mazurek, Acta Pol. Pharm. Drug Res. 71 (2013) 1073.
[2] R.C. Haddon, G.E. Scuseria, R.E. Smalley, Chem. Phys. Lett. 272 (1997) 38.
[3] A. Huczko, M. Bystrzejewski, Fulereny 20 lat później, Wydawnictwo Uniwersytetu Warszawskiego, Warszawa, 2007
[4] D. Steinhilber, M. Schubert-Zsilavecz, H.J. Roth, Chemia medyczna, MedPharm Polska, 2010
[5] W. Jańca, Kompendium farmakologii, PZWL, Warszawa, 2005
[6] Spartan’14, Wavefunction. Inc., Irvine, CA, 2014

The form of presentation proposed by the Author:
poster