SPATIAL MODELS OF GLUCOSE AND DI-GLUCOSE OPTIMIZED STRUCTURES

G.D. ABBASOVA, E.Z. ALIYEV, G.R. SAFARLI
Chair of optics and molecular physics, Baku State University,
Z. Khalilov st.23, AZ-1148, Baku, Azerbaijan

The spatial and electron structure of dextran-glucose monomer units is investigated by semiempirical methods of molecular mechanics and quantum chemistry with the help of computer calculative programs. Glucose and di-glucose complexes with iron oxide Fe_2O_3 are studied. The geometric parameters characterizing the energy-stable states of investigated compounds and their coordination complexes are calculated.

Keywords: dextran, glucose, di-glucose, iron oxide.
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INTRODUCTION

The nano-medicine which is new interdisciplinary direction including the control under biological systems on the base of nano-technology achievements, is the one of the priority directions of the modern medicine. The scientists all over the World work under development of technologies for nano-medicine field including first of all address delivery of medicines to affected cells (cancer cells; cells infected by virus; atherosclerotic plaques and etc), diagnostics with the help of quantum dots, chip laboratories, new antibacterial agents. The developed systems of medicine delivery are used practically in all fields of medicine: endocrinology, pulmonology, cardiology, oncology and etc. The investigations on construction of nano-devices, the implantation of which into human brain allows us to increase the human knowledge and rate of its thinking in many times, appear. Big successes in the field of gene therapy are achieved.

The modern nano-medicine has achieved the great success in the search and formation of new classes of medicines used in the therapy of cancer illnesses. Known that antineoplastic drugs have the low therapeutic indexes and their use efficiency is limited by high general toxicity, metabolic instability in organism and bad penetration into cancer cell. For the solution of these problems the carriers of anticancer drugs which defend the medicine from ferment influence and prevent their biological degradation in biological liquids, for example, in blood, are used. The principal possibility of liposome application as carriers of such medicines is shown in series of fundamental works. The substance including in liposome not only effectively assimilate the medicine but also causes to increase of medicine life-time because of its release from liposomes.

In the given work the spatial and electron structures of monomer unit dextran-glucose, di-glucose are investigated by methods of molecular modeling and empiric methods of quantum chemistry; their coordination complexes with iron oxide Fe_2O_3 are studied. The electron structures of glucose and di-glucose are calculated on the base of equilibrium nuclear configuration coordinates obtained as a result of molecule geometry optimization in potentials of semiempirical methods of molecular mechanics MM+. In molecular mechanics' methods the atoms are considered as Newtonian particles being in force field and interaction between them is described by potential energy. The potential energy depends on bond length, angles between bonds, dihedral angles of rotation round single bonds and on interaction of unbound molecular fragments with the help of electrostatic forces, Van-der-Waals forces or interactions causing the hydrogen bonds. There are different modifications of calculative programs ((MM+, AMBER, BIO and etc.) in the dependence on approximations used at calculation of force field and on harmonic functions describing this field.

CALCULATION METHODS

In the given work the calculations are carried out with the help of MM^+ method. Big database allows us to form the proteins, polymers, DNA fragments, metal clusters, modern systems of organometallic compound. The semiempirical methods of quantum chemistry in the dependence on use degree of zero differential overlap and approximation of core, Coulomb and exchange integrals included in matrix elements of Fock operator, have the different modifications. These methods MO CCП INDO/1,2,S, CNDO/1,2, MINDO/1,2,3, MNDO, AM1, PM3, MP2, Huckel method and series of other methods are well known. Each of methods allows us to obtain the series of either electron or spectral characteristics the values of which well coincide with the experiment in the result of calculation. In the work the calculations are carried out with the help of the PM3 method parameterized for the atoms of transition metals.

RESULTS AND THEIR DISCUSSION

The results of total energy calculation of glucose and di-glucose before and after molecule geometry optimization by MM^+ method are given in Table 1. The glucose total energy decreases on 16.13 kkal/mol, the di-glucose total energy decreases on 486.21 kkal/mol. These values also characterize the bonding energy in the investigated compounds. The changes in the values of electron energy are the essential ones:

131, H.Javid ave, AZ-1143, Baku
ANAS, Institute of Physics
E-mail: jophphysics@gmail.com

the decrease of electron energy on 828.46 kkal/mol is observed for glucose whereas for di-glucose the relative energy increases on 36747.21 kkal/mol. Correspondingly, the opposite picture is observed at comparison of nuclear repulsion energy: if in glucose the nuclear repulsion energy increases on 844.68 kkal/mol then in di-glucose this value is 37233.42 kkal/mol.

The one of the important molecule characteristics defining their behavior in the different force fields is the dipole moment having the additivity property. The optimized structure of di-glucose is characterized by the value of dipole moment 4.71D which on 1.39 D bigger than sum of dipole moments of glucose isolated molecules.

Table 1.

Calculation results by PM3 method data before (upper line) and after (low line) optimization

Molecule	Energy parameters, kkal/mol				Dipole moment, Debye
	Total energy	Electron energy	Nuclear repulsion energy	Bonding energy	
Glucose	-61301.29	-325723.21	264421.91	-2258.03	2.30
	-61317.42	-324894.75	263577.33	-2274.16	1.66
Di-glucose	-114656.53	-882892.67	768236.14	-3845.47	5.54
	-115142.74	-846145.46	731002.72	-4331.68	4.71

The geometric parameters characterizing the optimized spatial structure of di-glucose molecules are given in Table 2.

Table 2.

Parameters characterizing the low-energy state of di-glucose

Valence angle	**Value (degree)**
O_6-C_5-O_{12}	106.09
C_5-O_{12}-C_{30}	115.62
O_{12}-C_{30}-C_{24}	112.64
C_{30}-C_{24}-O_{29}	104.74
C_{30}-C_{24}-C_{25}	111.42
O_6-C_5-C_4	113.75
C_5-C_4-O_{11}	112.24
C_4-C_5-O_{12}	109.27
Torsion angle	**Value (degree)**
O_6-C_5-O_{12}-C_{30}	89.23
C_5-O_{12}-C_{30}-C_{24}	83.71
O_{12}-C_{30}-C_{24}-O_{29}	103.74
C_{30}-C_{24}-O_{29}-C_{28}	174.81
O_{12}-C_{30}-C_{24}-C_{25}	135.44
O_{11}-C_4-C_5-O_{12}	57.39
C_4-C_5-O_{12}-C_{30}	147.75
O_{29}-C_{28}-C_{27}-C_{26}	50.01
Bond	**Length (Å)**
C_5-O_{12}	1.42
O_{12}-C_{30}	1.41
C_{30}-C_{24}	1.56
C_{24}-O_{29}	1.43
C_{24}-C_{25}	1.55
O_{29}-C_{28}	1.41

In spite of the presence of different substituents of C_5 and C_{30} atoms, bond lengths C_5-O_{12} and C_{30}-O_{12} have practically the similar values which are equal to 1.4177 and 1.4129 Å, correspondingly. The torsion angle defining the glucose molecule orientation relatively each other has the value equal to 83.71^0, i.e. close to direct one.

As it is followed from calculation results, the decrease of negative charge value on oxygen atoms is observed as a result of transition of electron density

from p-orbitals of oxygen atoms on d-orbitals of iron atoms. The length of single bond of Fe-O is equal to 1.776 Å whereas the length of double bond of Fe=O is 1.4858 Å. The valence angle value of Fe-O-Fe which is equal to 76.4^0 provides the maximum good balance between electrostatic interactions of opposite charged atoms.

The results obtained in the given work can be used for construction of pharmacology medicines with potential therapeutic value and satisfying the wide range of qualitative criteria: high activity, high selectivity, minimal toxicity, high biological compatibility.

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