Analysis of the structure and vibrational spectra of glucose and fructose

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Abstract: Molecular modelling using semiempirical methods AM1, PM3, PM5 and, MINDO as well as the Density Functional Theory method BLYP/DZVP respectively were used to calculate the structure and vibrational spectra of d-glucose and d-fructose in their open chain, α-anomer and β-anomer monohydrate forms. The calculated data show that both molecules are not linear; ground state and the number for the point-group C is equal to 1. Generally, the results indicate that there are similarities in bond lengths and vibrational modes of both molecules. It is concluded that DFT could be used to study both the structural and vibrational spectra of glucose and fructose.

Keywords: FTIR; D-glucose; D-fructose; α-anomer; α-anomer; semiempirical calculations; density functional theory (DFT).

Introduction

Carbohydrates represent a very important class of compounds in biological systems and play a key role in many processes important to life[1-3]. Hydration of carbohydrates is an important point of research[4-5]. Spectroscopic parameters can be well determined using molecular modelling calculations. Molecular Mechanics (MM) can model very large compounds quickly[6]. Both Quantum Mechanics (QM) and (MM) are mixed to calculate several parameters for biological and many other systems[7-11]. The crystalline structures of α-D-Glucose, α-D-Glucose monohydrate and β-D-Glucose were studied by means of *ab initio* calculations[12]. The interaction between water and α/β-D-Glucose was studied by Density Functional Theory (DFT) B3LYP level[13]. Both α and β-D-

Glucose anomers were studied in gas phase and solution form using both DFT and *ab initio* calculations [14]. In the same way, molecular dynamics (MD) study of 1,5 anhydro-D-Fructose in aqueous solution have been carried out[15]. High-level DFT methods were used to study the conformational preferences of the $^4C_1$ and $^1C_4$ chair conformations as well as boat and skew–boat conformations of α- and β-D-Mannopyranose[16]. Generally vibrational spectroscopic method of analyses were found useful to characterize carbohydrates. The Raman optical activity of D-fructose in aqueous solution were reported[17]. Both physicochemical properties and vibrational spectra of small carbohydrates was studied to asses the role of water in sweet-taste of carbohydrate. So that, D-Fructose in water and alkali solutions were studied using Raman spectroscopy in the OH

stretching region[18]. Sequential injection Fourier Transform Infrared (FTIR) spectroscopy is presented as a fully automated method for the rapid determination of Glucose, Fructose, and Sucrose in soft drinks[19]. FTIR was also used to study the adsorption of Glucose monomer on hematite and quartz. The common adsorption mechanism indicated is a surface reaction involving the iron ion[20]. Glucose among other carbohydrate molecules were linked to maleic anhydride functionalized polystyrene by polymer analogous reactions to produce biodegradable polymers. FTIR spectra confirmed the degradation of the polymer[21].

On the basis of the above considerations, the present study aims to use molecular modelling together with the experimental measurements to study the structure and vibrational spectra of two important biological molecules, Glucose and Fructose in their open chain, α-anomer and β-anomer monohydrate structures. Molecular modeling calculations were conducted using Semiempirical methods, AM1, PM3, PM5 and MINDO. Furthermore, the DFT (BLYP/DZVP) was also used. The structure and vibrational spectra of the two molecules were calculated. The computed BLYP/DZVP frequencies were compared with those obtained experimentally by FTIR Spectroscopy

Experimental

α-D-Glucose and β-D-Fructose were purchased from Aldrich (molecular weight for each is 180.16) and were used without further purification. The FTIR spectra were collected for these samples using Fourier Transform IR spectrometer Nexus 670, Nicolet, USA. The number of scans was 32 and the resolution was 4 cm^{-1}. All spectra were collected in the range (4000-400 cm^{-1}). The KBr technique was used to prepare the samples for IR measurements.

Calculation details

Calculations were carried out on a personal computer using quantum mechanical methods as implemented with the MOPAC 2002 Version 1.33 CAChe Program (by Fujitsu). The geometry of Glucose and Fructose in their open chain, α-anomer as well as β-anomer monohydrate structures were optimized at Semiempirical methods AM1[22], PM3[22], PM5[23] and MINDO[24] as well as DFT method, Beck-Lee-Yang-Parr correlation functional, BLYP with the double zeta, DZVP basis set. For the DFT method, the vibrational spectra were performed after the harmonic approximation.

Results and Discussion

Optimized geometry: The calculations of geometry optimization locate the lowest energy molecular structure in close proximity to the specified starting structure[25-27]. The symmetry of the molecular structures as shown in Figure 1 corresponds to the C_1 point group. The two studied molecules reveal that they both have the same chemical formula, which is $C_6H_{12}O_6$. The open chain D-Glucose molecule in Figure 1-a starts with a CHO group bonded to four subsequent carbon atoms and each carbon atom carries a hydroxyl group and a hydrogen atom and the last carbon atom is bonded to methyl group CH_2OH. Similarly the open chain D-Fructose can be described as in Figure 1-d. In contrast to D-Glucose the structure of the optimized D-Fructose contains 4 carbon atoms between two methyl groups CH_2OH. The second carbon atom is bonded to an oxygen atom to form C=O while the rest of carbon atoms is carrying hydrogen atoms and hydroxyl groups. The flexibility of these open chain molecules together with the high reactivity of the CH_2OH and CHO groups lead to an internal cyclizations, as the carbonyl groups reacts with one of the hydroxyl groups from the other end of the molecule. As shown in Figure 1-b, the resulting ring contains 5 carbon atoms and one oxygen atom. The closure of the linear molecules to make a ring creates a new chiral center at C_1, called the anomeric carbon. When the hydroxyl group is attached to C_1, the carbon atom next to the ring oxygen and which does not carry the methyl group is in an axial or equatorial position with respect to the ring, these anomers are called α and β

anomers[12]. The bond distances C-C, C-H, O-H, C-O and C=O were calculated and presented in Tables 1 to 3. Regarding AM1, PM3, PM5 and MINDO results, there is a small variation in the calculated bond lengths as compared to BLYP/DZVP.

As can be seen in Table 3 the two molecules show comparable bond distances at the BLYP level of theory. The calculated bond lengths for D-Glucose are 1.537 Å, 1.120 Å, 0.984 Å, 1.455 Å and 1.235 Å for the bonds C-C of CH_2O, C-H, O-H, C-O and C=O respectively.
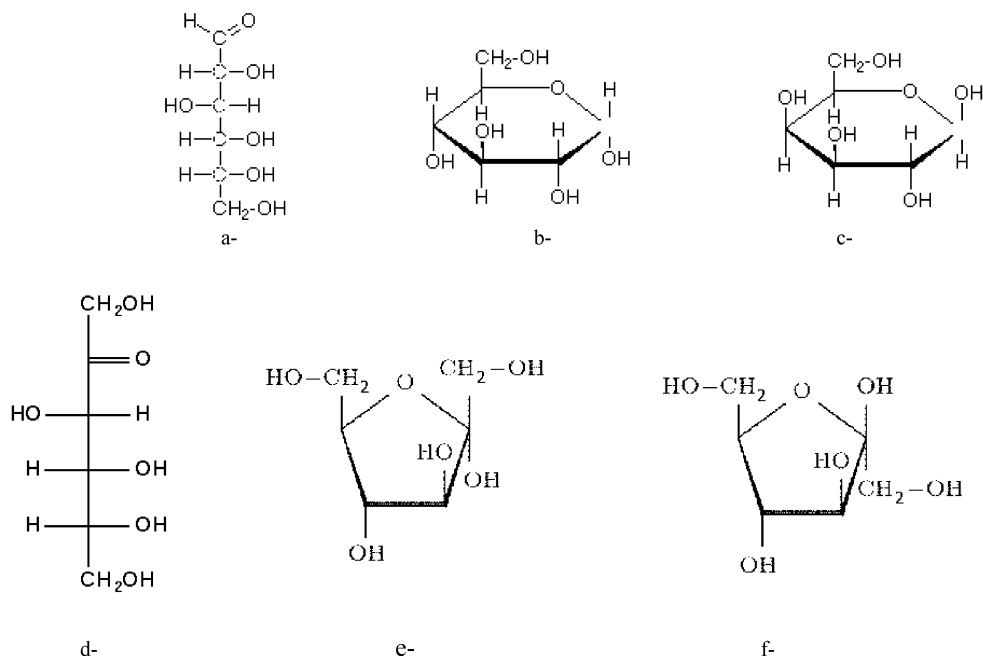
Figure 1. Structure of a- D-Glucose, b- α-D-Glucose, c- β-D-Glucose, d- D- Fructose, e- α-D-Fructose and f- β-D- Fructose.

Table 1. Calculated bond lengths in angstroms for D-Glucose and α-D- Glucose, which were optimized at the semiempirical AM1, PM3, PM5, MINDO as well as Density Functional method BLYP/DZVP levels of theory.

Bond Distance	AM1		PM3		PM5		MINDO		BLYP	
	D	α-D	D	α-D	D	α-D	D	α-D	D	α-D
C-C (CH_2O)	1.513	1532	1.531	1.544	1.539	1.559	1.554	1.577	1.537	1.532
C-C (Ring)		1.534		1.548		1.544		1.582		1.559
C-H	1.132	1.123	1.117	1.104	1.129	1.104	1.124	1.121	1.120	1.108
O-H	0.968	0.964	0.959	0.949	0.955	0.949	0.947	0.947	0.984	0.980
C-O	1.415	1.419	1.405	1.400	1.389	1.400	1.398	1.394	1.454	1.447
C=O	1.231		1.213		1.209		1.221		1.235	

D: Open chain D-Glucose, α-D: α-anomer Glucose

Table 2. Calculated bond lengths in angstroms for D-Fructose and α-D-Fructose, which optimized at the semiempirical AM1, PM3, PM5, MINDO as well as Density Functional method BLYP/DZVP levels of theory.

Bond Distance	AM1		PM3		PM5		MINDO		BLYP	
	D	α-D	D	α-D	D	α-D	D	α-D	D	α-D
C-C (CH$_2$O)	1.505	1.546	1.523	1.566	1.524	1.582	1.550	1.600	1.529	1.565
C-C (Ring)		1.536		1.570		1.587		1.610		1.562
C-H	1.123	1.122	1.105	1.108	1.120	1.119	1.120	1.123	1.110	1.106
O-H	0.967	0.964	0.950	0.948	0.955	0.953	0.947	0.947	0.987	0.980
C-O	1.410	1.416	1.398	1.405	1.389	1.393	1.390	1.392	1.428	1.452
C=O	1.236		1.216		1.214		1.223		1.243	

D: Open chain D-Fructose, α-D: α-anomer Glucose

Table 3. Comparison between bond lengths in angstroms for Glucose and Fructose which re calculated at the Density Functional Theory BLYP/DZVP level of theory.

| Bond Distance	Glucose			Fructose		
	D	α-D	β-D M	D	α-D	β-D M
C-C (CH$_2$O)	1.537	1.532	1.535	1.529	1.565	1.559
C-C (Ring)		1.559	1.559		1.562	1.560
C-H	1.120	1.108	1.113	1.110	1.106	1.105
O-H	0.984	0.980	0.980	0.987	0.980	0.978
C-O	1.454	1.447	1.450	1.428	1.452	1.449
C=O	1.235			1.243		

D: Open chain, α-D: α- anomer and β-DM: β-anomer monohydrate

Similarly the calculated distances for the same bonds for D-Fructose are 1.529 Å, 1.110 Å, 0.987 Å, 1.428 Å and 1.243 Å, respectively. Comparing between D-Glucose and D-Fructose structures one can observe a similarity in the calculated bond distances. As shown in Table 3 a slight change in the structure is noticed as a result of changing open chain into anomeric. Momany[13] studied the effect of hydration on the α-D Glucopyrnose. It is stated that, although monohydrated β-D Glucopyranose has only one-water molecule good geometries are obtained for this structure. It is proposed that, both of α and β anomers can be studied in its monohydrate form. At this level of theory α-anomer monohydrate is unstable and no optimal structure is found. On the other hand, the optimum structure of β-anomer monohydrate has been found. As seen in Table 3, it is clear that solution phase is slightly lower than gas phase. It seems to be that the molecules in gas phase are rearranged so that their bonds are enlarged slightly as compared with monohydrate structure.

Infrared spectra: Assignments of infrared frequencies are achieved by comparing of the band positions and intensities observed in IR spectra with wavenumbers and intensities from molecular modeling calculations. As seen in Table 4 there are similarities in vibrational spectra of both D-glucose and D-Fructose. The spectra can be assigned generally as in the following: The OH vibrational stretching is calculated to be in the region 3876 to 3005 cm^{-1}, then the CH vibrations up to 2061 cm^{-1}. The

C=O stretching is calculated from 1849 to 1634 cm^{-1}. A combination band of OCH and COH deformation is calculated from 1526 to 1347 cm^{-1}. Then the in plane CH and OH deformation from 1362 to 1191 cm^{-1} can be observed. A band of CO and CC stretching is regarded from 1191 to 995 cm^{-1}. The following spectra are assigned as
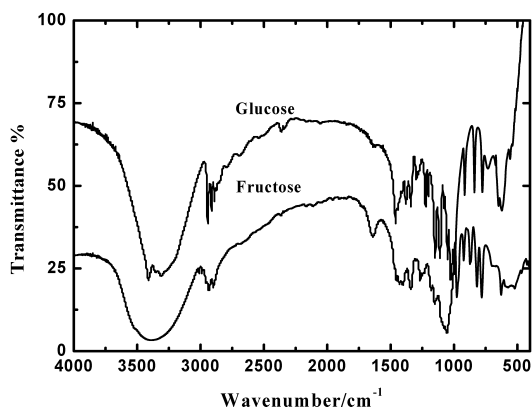
Figure 2. FTIR absorption spectra of both α-D-Glucose and β-D-Fructose.

CH deformation followed by CH2 vibration. As a general trend, Semiempirical methods AM1, PM3, PM5 and MINDO gave higher calculated frequencies as compared to scaled DFT method. This can be attributed to the effect of electron correlation, which is not included in semiempirical calculations.

To compare the calculated spectra with the experimental ones, FTIR Spectroscopy can be used to study the two molecules. Figure 2 shows the FTIR spectra of α-D-Glucose and β-D-Fructose respectively. Table 5 shows the assignment of the main characteristic absorption bands for each of two molecules. The vibrational spectra that indicated in both Figure 2 and Table 5 can be classified into two main groups of spectra. The region from 600 to 1500 cm^{-1} in which C-O and C-C groups vibration modes are present and the carbohydrates generally shows their characteristic bands. On the other hand the bands from 2900 to 3450 cm^{-1} assigned to CH and OH vibrations groups. α-D-anomer is tested with one water molecule (monohydrate form) and compared with both β-anomer as well as

Table 4. Calculated Infrared frequencies in cm^{-1} of the main characteristic absorption bands of open chain D-Glucose and D-Fructose.

AM1		PM3		PM5		MINDO		BLYP/DZVP	
D-G	D-F	D-G	D-F	D-G	D-F	D-G	D-F	D-G	D-F
3482	3500	3869	3876	-	3143	3994	3994	3453	3463
3460	3458	3768	3830	-	3118	3988	3252	3443	3005
3443	3020	3022	3020	3132	3043	3271	3185	2969	2953
2061	2059	1965	1973	1849	1841	2122	2127	1656	1634
1571	1577	1525	1460	-	1358	1526	1569	1456	1613
1430	1513	1408	1428	-	1352	1426	1537	1366	1392
1404	1444	1398	1406	1366	1337	1396	1441	1347	1320
1372	1322	1362	1307	1319	1332	1304	1354	1231	1276
1257	1300	1262	1268	1256	1254	1260	1292	1153	1148
1207	1279	1225	1244	1217	1222	1170	1214	1148	1093
1191	1161	1172	1227	1160	1149	1132	1140	1069	1001
1123	1066	1111	1159	1095	1076	1084	1092	1036	953
1060	1015	1016	1085	1000	1019	1017	1018	954	856
963	974	947	911	946	951	953	978	842	816
926	957	897	884	887	890	798	965	770	784
797	793	740	753	751	746	760	768	625	651

D-G: Open chain D-Glucose and D-F:Open chain D-Fructose.

Table 5. Comparisons between both experimental and BLYP calculated Infrared frequencies in cm^{-1} for both α- D-Glucose and β-D-Fructose as well as α- D-Glucose and β-D-Fructose monohydrates.

D-Glucose				D-Fructose			
IR	α-D	β-D-M	Assignment	IR	α-D	β-D-M	Assignment
3410	3418	3146	ν OH	3393	3428	3513	ν OH
3393	3408	3123	ν OH	2933	2975	2957	ν$_s$ CH of C2
2944	2963	3099	ν$_s$ CH of C2	2899	2923	2925	ν$_{as}$ CH of C1
2913	2939	3085	ν$_{as}$ CH of C1				
1460	1441	1465	δCH$_2$+ δOCH + δCCH	1637	1634	1665	δOH
1382	1352	1390	δOCH+ δ COH + δ CCH	1402	1392	1417	δOCH+ δ COH + δ CCH
1340	1333	1320	δ CCH+ δ OCH	1340	1320	1338	Δ CCH+ δ OCH
1224	1218	1278	δCH+ δOH in plane	1265	1276	1292	δOH in plane, δ CCO
1203	1220	1232	δCH+ δOH in plane				
1149	1137	1205	ν CO + ν CC	1149	1148	1166	ν CO+ νCC + δ CCC
1111	1116	1162	ν CO	1057	1082	1059	νCO
1050	1058	1088	ν CO + ν CC	977	990	990	νCO+ δCCO
1025	1026	1066	ν CO	923	943	951	νCO+ νCCH+ ν$_{as}$ ring of pyranose
995	944	1032	ν CO + ν CC	873	856	908	δCH + νCC+ δCCH
915	900	993	ν CO+ν CCH+ ν$_{as}$ ring of pyranose	818	816	884	δCH
837	834	909	δCH	780	784	828	δCCO+ δCCH
776	762	815	δ CCO+ δ CCH	627	644	658	CH$_2$ + CH
622	619	694	CH$_2$				

FTIR: Experimental frequencies, α-D: α -D-anomer, β-DM: β -D-anomer monohydrate.

experimental FTIR frequencies for α-D-anomer. It is worth to mention that, the β-D-anomer assignment is in a good agreement with that presented by Guo and Zhang[28]. Regarding the results of α-D-anomer, it is clear that the computed frequencies are in a good agreement with experimental ones except for CH and OH region. But there is agreement in the characteristic region of carbohydrate. In this region, there is a good correlation between both α and β anomer in one hand and the experimental frequencies on the other. The computed frequencies of α-anomer for both Glucose and Fructose are in a good agreement with experimental frequencies for both carbohydrate region as well as OH and CH region. Comparing computed and the experimental frequencies one can conclude that, accurate results could be achieved with scaled DFT method BLYP/DZVP with higher computation time as compared to semiempirical methods.

Conclusions

In the present study molecular models for two biological molecules, Glucose and Fructose are presented on the basis of Semiempirical and DFT calculations. The models present the structure and vibrational spectra for D-Glucose and D-

Fructose in their open chain, α-anomer and β-anomer monohydrate forms. The obtained result indicates that there are similarities in the structural and vibrational characteristic of both molecules. Although monohydrate α-anomer is not a complete hydration structure, its computed IR spectra is in a good agreement with experimental spectra for β-D-Fructose. In addition, the computed spectra for α-D-Glucose monohydrate are in a good agreement with experimental one in the characteristic region (600 – 1500 cm^{-1}) and far from it in the OH region. It can be concluded that with a comparable results and lower computation time, semiempirical method could be used to study carbohydrates such as Glucose and Fructose. On the other hand for accurate and precise structural and vibrational data DFT method could be used with a good agreement with experimental results.

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