Density functional theory study of N–H···O=C hydrogen-bonding effects in structure of beta amyloid (Aþ): ^{17}O and ^{14}N nuclear quadrupole resonance parameters

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Introduction

The þ-amyloid proteins (Aþ), especially the variant Aþ1-42, are the primary constituent of the amyloid plaques which are characteristic of Alzheimer's disease. Amyloid fibrils [1] are composed of cross-þ-sheets (i.e. the constituent þ-strands run perpendicular to the fiber axis). Hydrogen bonds (HBs) play a fundamental role in amyloid fibrils formation. Because hydrogen-bonding interactions are mainly electrostatic in nature, the techniques that deal with the charge distribution around the nuclei seem to be reliable techniques to characterize the nature of hydrogen bonds. Nuclear quadrupole resonance, NQR, spectroscopy is well-established as a versatile technique to study the details of the electronic and nuclear charge distribution around the nucleus of interest [2-3].

The quantum mechanical approaches have shown to be a very effective method in determination of charge distribution. It permits to estimate the electric field gradient (EFG) resulting from the whole molecular charges around nucleus. As for the high sensitivity to the electrostatic environment of nuclei, electronic structures and intermolecular interactions, such as hydrogen bonding (HB), can produce a significant influence on the EFG tensors. EFG is a traceless, symmetric second-rank tensor whose principal axes system (PAS) are chosen so that its components satisfy $|q_{zz}| \leq |q_{yy}| \leq |q_{xx}|$ ($q_{ij} = 6\ ^2V/6_i6_j$) where i, j = x, y, and z, and V is the external electrostatic potential. The nuclear quadrupole coupling constant (NQCC) and asymmetry parameter (4_Q) are those quantities determined experimentally by NQR. NQCC means the interaction energy between electric quadrupole moment, eQ, of nucleus and the EFG tensors arisen at the site of quadrupolar nucleus (Those nuclei with spin angular momentum greater than one-half (I>1/2) are quadrupole). 4_Q parameter

measures the EFG tensors deviation from cylindrical symmetry at the site of quadrupolar nucleus.

Keywords: þ-amyloid; DFT; NQR; Electric field gradient; N–H···O=C hydrogen-bonding

Computational details

All quantum chemical calculations on ^{17}O, ^{14}N EFG tensors were carried out with the GAUSSIAN 98 package. Among the various functionals for density functional theory (DFT) calculation, B3LYP with the 6-31+G* standard basis set were used. Because amyloid fibrils are inherently noncrystalline and insoluble, determination of their molecular structures by the two principal experimental approaches to structure determination, i.e., X-ray crystallography and liquid-state nuclear magnetic resonance (NMR), has not been possible. Since the positions of atoms are determined accurately by solid-state NMR, no geometry optimization was needed in this work.

The calculated principal EFG components, q_{ii}, were used to obtain the nuclear quadrupole coupling components from the equation: NQCC [MHz] = e^2Qq_{zz}/h = -2.3496Q[fm^2]q_{zz}[au] where eQ is the nuclear electric quadrupole moment and the coefficient of 2.3496 arises from the unit conversion. Asymmetry parameter defined as, 4_Q = ▌(q_{yy}-q_{xx}) / q_{zz} ▌, 0≤ y ≤1.

The standard values of quadrupole moment, eQ, reported by Pyykkö [4] were used, consequently: eQ(^{17}O) = -2.558 fm^2 and eQ(^{14}N) = 2.044 fm^2.

Result and discussion

In the present study, we calculated ^{17}O and ^{14}N EFG tensors of Aþ for residues 23-27 to investigate the influence of intermolecular hydrogen-bonding interactions. To achieve the aim, the calculations were performed for two molecular models including an isolated gas phase (monomer) and a dimer form; see Figure 1 for details.

Figure 1 presents the intermolecular hydrogen bonds formed between N—H of one strand and C=O of another. As the results of Tables 1 illustrates, due to the hydrogen bonding interactions, ^{14}N nuclear quadrupole coupling constants and asymmetry parameters deviate significantly from the monomer values. More specifically, hydrogen-bonding interactions cause a 0.673 MHz reduction in NQCC (^{14}N) parameter

for ^{14}N nucleus involved in R $_{26,27}$ residue. As also shown in Table 2, the results of ^{17}O quadrupole coupling constants and asymmetry parameters show some degree of sensitivity upon the O=CNH···O=CNH hydrogen-bonding environment. These results reveal the significance of including the hydrogen-bonding interaction in determining the ^{14}N and ^{17}O quadrupole coupling tensors in Aþ.

References:

1. T. Luhrs, 3D Structure of Alzheimer's Aþ (1-42) fibrils, PNAS. 102 (2005) 17342-17347.
2. B. Nogaj, Hydrogen-bond theories and models based on nuclear quadrupole resonance spectroscopy studies, J. Phys. Chem. 91 (1987) 5863–5869.
3. M. J. Hunt, A. L. Mackay, Deuterium and nitrogen pure quadrupole resonance in amino acids. II, J. Magn. Reson. 22 (1976) 295–301.
4. P. Pyykkö, Spectroscopic nuclear quadrupole moment, Mol. Phys. 99 (2001) 1617–1629.

Table 1. Calculated quadrupole coupling constants and asymmetry parameters of ^{14}N nuclei in residue 23-27.

Model	Nucleus between residue i , j	NQCC (MHz)	4_Q
Monomer	R 23,24	3.853	0.073
	R 24.25	3.867	0.242
	R 25,26	3.834	0.105
	R 26,27	4.411	0.145
Dimer	R 23,24	4.013	0.278
	R 24,25	3.641	0.098
	R 25,26	3.567	0.311
	R 26,27	3.738	0.119

Table 2. Calculated quadrupole coupling constants and asymmetry parameters of ^{17}O nuclei in residue 23-27.

Model	Nucleus between residue i , j	NQCC (MHz)	4_Q
Monomer	R 23,24	8.634	0.182
	R 24.25	8.591	0.192
	R 25,26	8.412	0.214
	R 26,27	9.665	0.132
Dimer	R 23,24	8.990	0.089
	R 24,25	8.283	0.244
	R 25,26	8.969	0.174
	R 26,27	9.494	0.181

Figure 1. Dimer structure of residues 23-27 in Aþ. (red:O, blue:N, green:C, gray:H)