QUARKS: Brazilian Electronic Journal of Physics, Chemistry and Material Science
journal homepage:
https://periodicos.ufjf.br/index.php/quarks
e-ISSN: 2674-9688

| Vol 2 | | No. 2 | | March 2020 |

Theoretical Studies of Milk: Solvent Effects on the Molecular Properties of Retinoid Compounds

Geórgia Maria A. Junqueira[a] (junqueira.georgia@gmail.com), Renata Carvalho Teixeira[a] (renata_teixeira@id.uff.br), Leandro da Conceição Luiz (livroleandro@gmail.com), Maria Jose V. Bell[a] (mjbell06@gmail.com) and Virgílio de Carvalho dos Anjos[a] (virgilio.anjos@gmail.com)

[a]Departamento de Física, Universidade Federal de Juiz de Fora, Juiz de Fora, 36036-900, Brasil)

DOI: https://doi.org/10.34019/2674-9688.2020.v2.28632

Abstract

We discuss here the role of environment in the structural and spectroscopic properties of vitamin A in its retinoid forms: retinol and retinal. The analyzed compounds show three singlet excited states exhibiting wavelengths between 472 and 273 nm according to the medium. The transitions involve HOMO, LUMO, HOMO-1, LUMO and HOMO, LUMO+1 orbitals.

Keywords: DFT, PCM, milk, vitamin A.

*Corresponding author. E-mail: junqueira.georgia@gmail.com

1. Introduction

Cow milk (consisting of water, fatty acids, proteins, sugars, minerals and vitamins) is the one of the most consumed food of the world [1]. Vitamin A, naturally found in milk, includes diverse retinoid and carotenoid compounds. All forms of vitamin A have in common a beta-ionone ring to which one chromophore, the retinyl group [CH_2=C(CH_3)-CH=CH_2].

Investigations involving milk quality control are extremely important for the dairy industry once it aims to protect the health of producers and consumers. Moreover, the identification and the use of molecular markers for milk quality studies assure benefits and better productivity [2].

Theoretical calculations are a powerful tool being able to predict, propose and validate experiments, mainly in complex systems as milk. In this context the Tomasi's polarizable continuum solvation model (PCM) [3, 4] represent a solvated molecule inside a molecule-shaped electrostatic cavity surrounded by a dielectric medium (solvent).

In addition, Time-Dependent Density Functional Theory (TD-DFT) [5] is a well-established method widely used for calculating excitation energies [6].

Vitamin A has been employed as a spectroscopic marker in milk [7-10]. Fatty acids [7] and β-lactoglobulin protein [9,10] present in milk have been related with specific changes in the electronic spectrum and fluorescence of this vitamin. However, it is still an open question. What kind of effects is responsible for such spectroscopic data? What are the molecular structures involved in this process? With the aim of expanding this theme and future practical uses, we investigate, by means of TD-DFT/PCM approach [5], the electronic behavior of some molecules associated with vitamin A- retinol and retinal- in different solvents. In order to include solute-solvent interactions in the calculations, a quantum mechanical operator derived from PCM was employed [11]. It depends on the solute electronic density being used to modify the TD-DFT equations to find the electronic transition energies in solution.

This paper was organized as follows: In the next section, we describe the theoretical methods to calculate the electronic spectroscopic data. The results were presented and discussed in Section 3, and the final remarks were summarized in the last Section

2. Metodology

The geometries of considered molecules were fully optimized at B3LYP/6-31+G(d,p) level of theory in the gas phase and in the presence of the solvent. By means of Time-Dependent DFT (TD-DFT) [5,11] using B3LYP/6-31+G(d,p) the absorption spectra were obtained. In addition, the energies of the frontier orbitals, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), as well as the density of states (DOS) were found. The medium effects were included using the dielectric polarizable continuum model (PCM) [3,4]. All calculations were performed with Gaussian03 [12] computational package.

3. Results and Discussion

The molecular properties calculations were carried in vacuum (ε=1.0) and some solvents: benzene (ε=2.3), acetonitrile (ε=36.6) and water (ε=78.5), where ε are the respective dielectric constants, with the polarizable continuum model (PCM) [4]. The optimized geometries of retinol and retinal can be visualized in **Figure 1** and the structural parameters are reported in **Table 1**. There are no significant alterations among the isolated and in solution geometries.

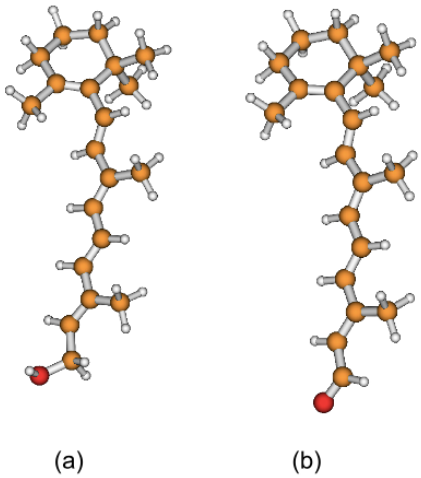


Figure 1. B3LYP/6-31+G(d,p) optimized geometries of retinoid compounds (a) retinol and (b) retinal.

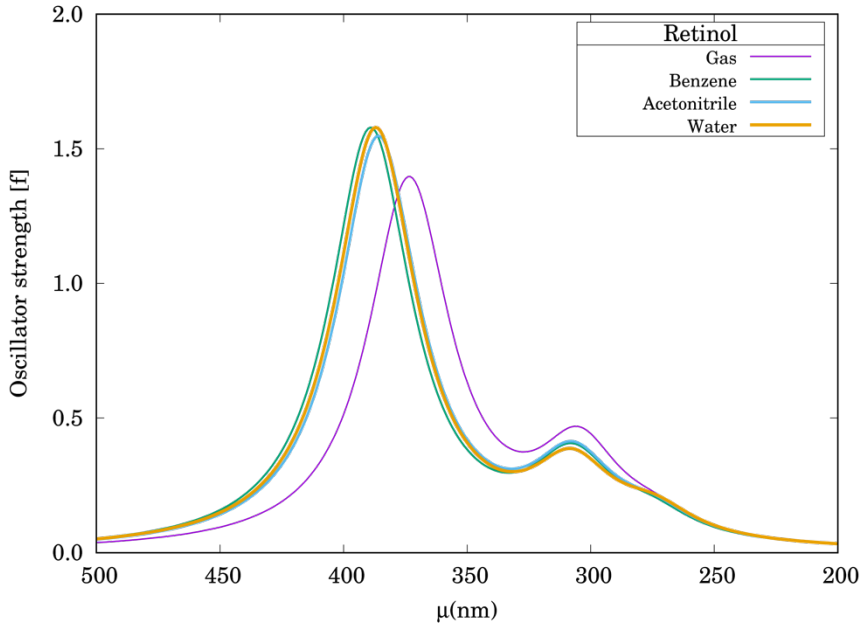
Table 1: Structural data average (Å) obtained at B3LYP/6−31G level of theory.

	Retinol	Retinal
C−C (ring)	1.495±0.07	1.533±0.01
C−H (ring)	1.114±0.07	1.097±0.003
C-C (methyl)	1.526±0.02	1.526±0.02
C-H (chain)	1.091±0.004	1.091±0.007
C−O	1.495±0.07	1.495±0.07
O−H	0.967	–

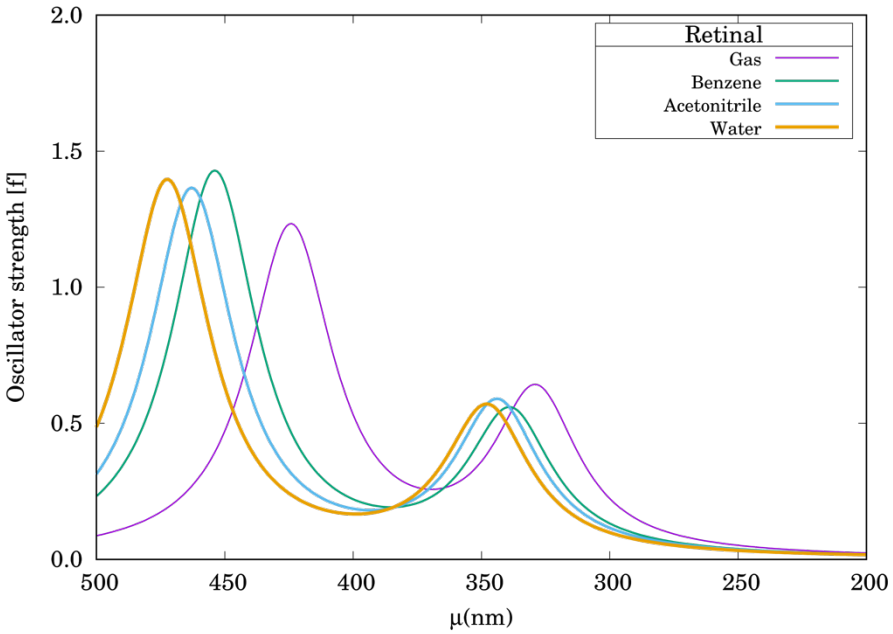
Table 2: Electronic transitions obtained in gas phase and solutions for the studied compounds. TD-DFT calculations: wavelengths λ, oscillator strengths [f] and dipole moments.

	Electronic transitions			Dipole
	/nm[f]	/nm[f]	/nm[f]	Debye
	HOMO, LUMO	HOMO-1, LUMO	HOMO, LUMO+1	
		Retinol		
vacuum (ε=1.0)	374[1.4]	305[0.34]	274[0.07]	2.6631
benzene (ε=2.3)	389[1.6]	307[0.29]	275[0.08]	2.8303
acetonitrile (ε=36.6)	386[1.5]	307[0.30]	274[0.09]	2.9421
water (ε=78.5)	387[1.6]	308[0.30]	274[0.10]	2.8471
		Retinal		
vacuum (ε=1.0)	424[1.2]	403[0.0002]	329[0.59]	7.1163
benzene (ε=2.3)	454[1.4]	392[0.0001]	339[0.52]	8.2911
acetonitrile (ε=36.6)	463[1.4]	380[0.0001]	344[0.55]	9.8011
water (ε=78.5)	472[1.4]	373[0.0002]	348[0.54]	10.7029

The time-dependent spectroscopic properties for retinol and retinal was summarized in **Table 2**. The electronic spectra are shown in **Figure 2**. The studied molecules present three electronic excitations being one more intense, (π,π*) [13].



(a)

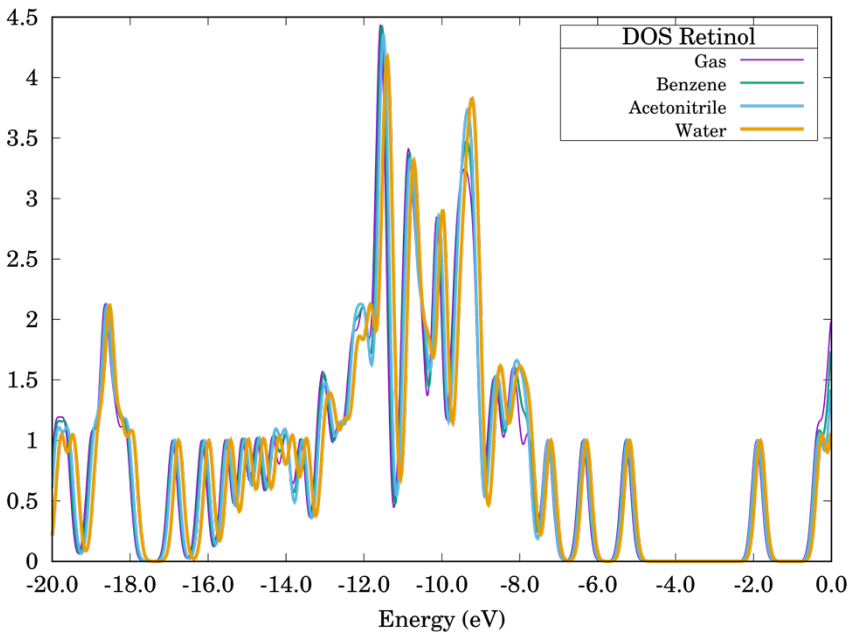


(b)

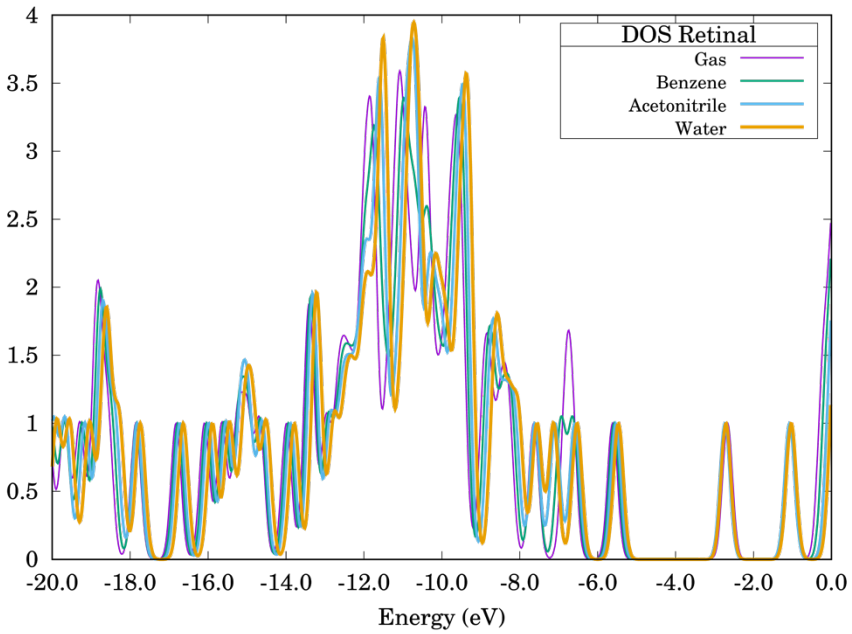
Figure 2: UV-Vis absorption spectra of (a) retinol and (b) retinal obtained in the vacuum and in some solvents.

According to **Figure 2** the UV-Vis spectra of retinol and retinal have different profiles. Regarding retinol, the solvent causes displacements (close to 15nm) of the transitions to regions of greater wavelengths. Moreover, the intensity (given by the oscillator strength) of the first electronic transition is enhanced (until by 12%), while the second is slightly decreased by the influence of the different environment. In the other hand, the polarity of the medium strongly and sequentially affects the UV-Vis spectra of retinal. There, as more polar the medium (higher dielectric constant), the greater the shift to red regions. The effects of hydration and solubility of retinol and retinal on the absorption spectra properties have been studied [14]. In fact, bathochromic shifts are observed from pure retinoids compared to water/ethanol solutions [14]. Experimental measures recorded in the non-polar solvents have detected maximum absorptions of 325-333 nm to retinol and 369-385 nm to retinal [15]. Our calculated values, considering solvents with low dielectric constants, were found 374-389 nm and 424-454 nm to retinol and retinal molecules, respectively. However, we are not interested in concordance with absolute experimental values. In contrast, the present study is to evaluate the influence of solvent in the absorption spectra profile of retinoids. We further explored the system's states by calculating the density of states (DOS) (**Figure 3**).

The electronic transitions computed are verticals and singlet-singlet type, between 472 and 273 nm. As can be noticed, all the excitations have almost the same energetic distribution. Both to retinol and retinal DOS data, the band gap occurs close to 4 eV in gas phase and in solution. If we consider that the strength of the solute-solvent interaction determines how much the band gap of the solvated solute deviate from that of its isolated form, it can be evaluated than solvent effects on the retinal spectra are more pronounced among them.



(a)



(b)

Figure 3: Density of States (DOS) plots for (a) retinol and (b) retinal carried in the vacuum and in solution.

4. Conclusions

In this paper we emphasize the idea of the vitamin to be used as a natural spectroscopic marker in milk. Considering the two retinoid compounds in gas phase and in solution, the structures in common to both remained practically unchanged. However, the electronic spectra are different from each other and very sensitive to the change of the medium. Our investigations show that the polarity of solvent has strong effect in the time-dependent spectroscopic properties of retinol and retinal.

Acknowledgments

The authors would like to acknowledge Universidade Federal de Juiz de Fora – UFJF by the visiting professor program, and thanks CAPES, CNPQ and FAPEMIG for financial support.

References and Notes

[1] E. M. Wiseman, S. B. Dadon, R. Reifen, The vicious cycle of vitamin a deficiency: A review, Critical Reviews in *Food Science and Nutrition* 57 (2017) 3703–3714.

[2] Singh, R. Deb, R. R. Alyethodi, R. Alex, S. Kumar, S. Chakraborty, K. Dhama, A. Sharma, Molecular markers and their applications in cattle genetic research: A review, Biomarkers and Genomic Medicine 6 (2014) 49 – 58.

[3] M. Cossi, V. Barone, Solvent effect on vertical electronic transitions by the polarizable

continuum model, *The Journal of Chemical Physics* 112 (2000) 2427–2435.

[4] J. Tomasi, B. Mennucci, R. Cammi, Quantum mechanical continuum solvation models, *Chem. Rev*. 105 (2005) 2999.

[5] C. Adamo, D. Jacquemin, The calculations of excited-state properties with time-dependent density functional theory, *Chem. Soc. Rev*. 42 (2013) 845–856.

[6] M. Casida, M. Huix-Rotllant, Progress in time-dependent density-functional theory, Annual Review of Physical Chemistry 63 (2012) 287–323.

[7] M. P. Brandão, M. G. Neto, V. de Carvalho dos Anjos, M. J. V. Bell, Detection of adulteration of goat milk powder with bovine milk powder by front-face and time resolved fluorescence, Food Control 81 (2017) 168 – 172.

[8] M. P. Brandão, G. M. A. Junqueira, M. J. V. Bell, V. de Carvalho dos Anjos, Time resolved fluorescence spectroscopy for ranking of milk powder nd substitutes, (2019) *on preparation*.

[9] F. Zsila, Z. Bikádi, M. Simonyi, Retinoic acid binding properties of the lipocalin member Î²-lactoglobulin studied by circular dichroism, electronic absorption spectroscopy and molecular modeling methods 64 (2003) 1651–60.

[10] D. Agudelo, P. Bourassa, J. Bariyanga, H. Tajmir-Riahi, Loading efficacy and binding analysis of retinoids with milk proteins: a short review, *Journal of Biomolecular Structure and Dynamics* 36(16) (2018) 4246-4254.

[11] M. Cossi, V. Barone, Time-dependent density functional theory for molecules in liquid solutions, *The Journal of Chemical Physics* 115 (2001) 4708–4717.

[12] Gaussian 03, Revision B.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2003.

[13] R. R. Birge, J. A. Bennett, B. M. Pierce, T. M. Thomas, Two-photon spectroscopy of the visual chromophores. evidence for a lowest excited 1Ag--like .pi..pi.* state in all-trans-retinol (vitamin a), *Journal of the American Chemical Society* 100 (1978) 1533–1539.

[14] E. Z. Szuts, F. I. Harosi, Solubility of retinoids in water, Archives of Biochemistry and Biophysics 287 (1991) 297 – 304.

[15] K. Chihara, W. H. Waddell, Electronic and vibrational spectral investigation of the molecular association of the all-trans isomers of retinal, retinol, and retinoic acid, *Journal of the American Chemical Society* 102 (1980) 2963–2968.