

Computational molecular characterization of the flavonoid Morin and its Pt(II), Pd(II) and Zn(II) complexes

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Abstract In this work, we make use of a model chemistry within density functional theory (DFT) recently presented, which is called M05-2X, to calculate the molecular structure of the flavonoid Morin and its Pt(II), Pd(II) and Zn(II) complexes, as well to predict their IR and UV-Vis spectra, the dipole moment and polarizability, the free energy of solvation in different solvents as an indication of solubility, the HOMO and LUMO orbitals, and the chemical reactivity parameters that arise from Conceptual DFT. The calculated values are compared with the available experimental data for these molecules.

Keywords Conceptual DFT · $\Delta G(\text{solv})$ ·
Molecular structure · Morin · Polarizability

Introduction

There is no doubt that among the large number of natural products of plant origin, debatably called secondary metabolites because their importance to the ecophysiology of the organisms that accumulate them was not initially recognized,

flavonoids play a central role. These compounds and their derived pigments have contributed to shaping our knowledge of modern genetics, providing colorful tools to investigate a number of central plant problems, including the biology of transposons, the regulation of gene expression, gene silencing, and the organization of metabolic pathways. The legacy left by several outstanding chemists who have devoted their lives to the understanding of the chemistry of flavonoids is being carried on by a growing number of scientists who take interdisciplinary approaches to continue to advance our knowledge of the pathway and develop new means to manipulate the synthesis of these compounds, which have significant potential in providing solutions to plant and animal illnesses alike [1–6].

Theoretical investigations of the physical and chemical properties of flavonoids are very important in order to disclose the relationship between the structure, properties and performance, and to help in the design and synthesis of new derivatives with improved properties. We have experimentally found that some natural flavonoids have a strong ability for complexing metal ions, in particular, those related to heavy metals. Thus, natural flavonoids could be useful in water treatment, cleaning and purification [7–10].

The objective of this paper is to report the results of the calculation of the molecular structure and properties of the flavonoid Morin and their Pt(II), Pd(II) and Zn(II) complexes using a recently developed density functional [11]. Besides the IR and UV-Vis spectra, the dipole moment and polarizability, the free energy of solvation in different solvents as an indication of solubility, the HOMO and LUMO orbitals, and the chemical reactivity parameters that arise from Conceptual DFT [12, 13] are reported. The calculated values are compared with the available experimental data for these molecules as a means of validation of the chemistry model used.

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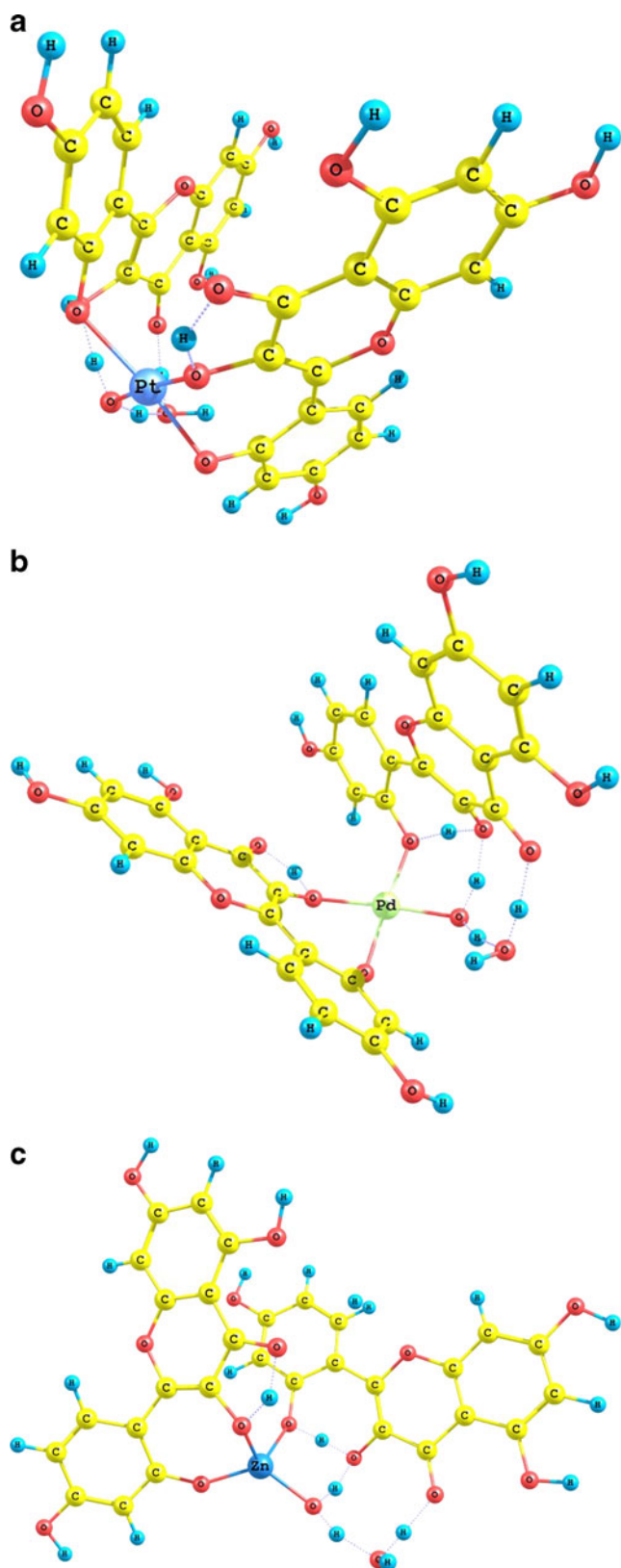


Fig. 2 Molecular structure of the Pt(II), Pd(II) and Zn(II) morin complexes calculated with the M05-2X/LANL2DZ model chemistry

Results and discussion

The results for the equilibrium conformation of the neutral molecule of the morin flavonoid calculated with the M05-2X/6-31+G(d) model chemistry are presented in Fig. 1 through a representation of the molecular structure showing the atomic labeling and numbering as well as the interatomic bond lengths and angles. It is interesting to note that there is H bonding between O29 and H16, with a length of 1.572 Å. The molecular structures of the Pt(II), Pd(II) and Zn(II) complexes of the morin flavonoid calculated with the M05-2X/LANL2DZ are presented in Fig. 2.

The most intense calculated frequencies in the infrared spectrum (IR) for the morin molecule calculated with the M05-2X/6-31+G(d,p) model chemistry are: 304.1 cm^{-1} =O11-H12 rocking, 370.1 cm^{-1} =O31-H32 rocking, 419.9 cm^{-1} =O29-H30 rocking, 473.8 cm^{-1} =O13-H14 rocking, 961.1 cm^{-1} =C25-H28 stretching, 1095.1 cm^{-1} =C2-O17 stretching, 1165.3 cm^{-1} =C-H rocking, 1186.7 cm^{-1} =C25-H28, O29-H30 rocking, 1188.3 cm^{-1} =O13-H14, C8-H10, O11-H12 rocking, 1231.6, 1242.9, 1267.6, 1318.9 cm^{-1} =C-H rocking, 1520.9 O15-H16-O29 waving, 1679.6 cm^{-1} =C6-C9, C3-C7 stretching, 1714.8 cm^{-1} =C21-C23, C22-C25 stretching, 1170.4 cm^{-1} =C18-O19 stretching, 3114.5 cm^{-1} =O15-H16 rocking, and 3643.2 cm^{-1} =O29-H30 rocking.

The most intense calculated frequencies in the infrared spectra for the morin-Pt(II), morin-Pd(II) and morin-Zn(II) complexes calculated with the M05-2X/LANL2DZ model chemistry are related to internal H-bonds, and the transitions can be assigned as follows: 2068.9 cm^{-1} =O9-H69-O37 as st, 2359.2 cm^{-1} =O8-H68-O5 as st, 2467.2 cm^{-1} =O9-H69-O37 rocking, 2666.8 cm^{-1} =O6-H67-O2 as st, 3035.8 cm^{-1} =O2-H3-O8 as st, and 3301.6 cm^{-1} =O41-H7-O6 as st, for the Pt(II) complex, 2095.5 cm^{-1} =O8-H36-O36 as st, 2357.1 cm^{-1} =O7-H67-O4 as st, 2471.3 cm^{-1} =O8-H36-O36 rocking, 2692.6 cm^{-1} =O5-H66-O1 as st, 3068.2 cm^{-1} =O1-H2-O7 as st, and 3309.5 cm^{-1} =O5-H6-O40 as st, for the Pd(II) complex, and 2096.8 cm^{-1} =O8-H68-O36 as st, 2181.8 cm^{-1} =O1-H66-O5 and O4-H67-O7 rocking, 2431.1 cm^{-1} =O4-H67-O7 as st, 2880.7 cm^{-1} =O1-H66-O5 as st, 3198.9 cm^{-1} =O1-H2-O7 as st, and 3375.5 cm^{-1} =O5-H6-O40 as st, for the Zn(II) complex.

The ultraviolet spectra (UV-Vis) of the morin flavonoid molecule and the Pt(II), Pd(II) and Zn(II) complexes calculated with the M05-2X/6-31+G(d,p) and the M05-2X/LANL2DZ model chemistries are presented by showing the principal transitions in Tables 1, 2, 3 and 4. The wavelength belonging to the HOMO-LUMO transition will take place at 286.2 nm for the morin flavonoid, while it will take place at 389.1, 382.3 and 406.7 nm for the Pt(II), Pd(II) and Zn(II) complexes, respectively.

The molecular dipole moment is perhaps the simplest experimental measure of charge distribution in a molecule.

Table 1 Electronic transition states of morin (nm, eV, oscillator strengths (f), and transition assignments as calculated with TD-DFT and the M05-2X/6-31+G(d,p) level of theory

Number	nm	eV	(f)	Assignment; H = HOMO, L = LUMO
1	345.9	3.58	0.0028	S H-3 → L+0(+62%) H-3 → L+2(+5%)
2	286.2	4.33	0.4672	S H-0 → L+0(+83%)
3	251.7	4.93	0.0069	S H-0 → L+1(+51%) H-2 → L+0(+13%) S H-1 → L+0(+9%) H-4 → L+0(6%)
4	247.4	5.01	0.0278	S H-0 → L+2(+31%) H-2 → L+0(+19%) S H-0 → L+1(14%) H-4 → L+0(+8%)
5	234.6	5.29	0.0874	S H-1 → L+0(+53%) H-2 → L+0(24%)
6	224.6	5.52	0.3487	S H-0 → L+2(+40%) H-2 → L+0(24%) S H-0 → L+1(+9%) H-1 → L+0(8%)

The accuracy of the overall distribution of electrons in a molecule is hard to quantify, since it involves all the multipoles. The polarizability α contributes to the understanding of the response of the system when the external field is changed, while the number of electrons N is kept fixed. The polarizability is calculated as the average of the polarizability tensor $\langle \alpha \rangle = \frac{1}{3}(\alpha_{xx} + \alpha_{yy} + \alpha_{zz})$. The results for the total energy (in a.u.), the dipole moment (in Debye) and the total polarizability (in Bohr³) calculated with M05-2X/6-31+G(d,p) and the M05-2X/LANL2DZ model chemistries and for the morin flavonoid and the Pt(II), Pd(II) and Zn(II) complexes are presented in Table 5.

The pKa of hydrogen atoms attached to oxygen atoms is calculated using the MOPAC 2009 program [26]. In this program, the pKa is calculated using the O-H distance calculated using PM6 [27], and a charge calculated using a method specifically designed to reproduce the charge for pKa. The results for the pKa of different hydrogen atoms in the morin molecule are: H12=7.207, H14=7.084, H16=11.619, H30=5.696, and H32=7.876. It should be recalled that the H16 is that involved in the internal H bonding mentioned earlier.

The free energy of solvation $\Delta G(\text{sol})$ of the molecule have been calculated for morin by resorting to the M052-2X/6-31+G(d,p) model chemistry coupled with the integral-equation-formalism of the polarized continuum model (IEF-PCM) for different solvents as implemented in Gaussian 03. The

solubility of a molecule will depend on several kinetic and thermodynamic factors. However, it can be said that the magnitude and the sign of $\Delta G(\text{sol})$ could be a good approximation as an index of solubility. In this way, a negative sign and a large magnitude will be an indication of increased solubility. The results of these calculations for the studied molecule can be summarized as follows: Acetone = -20.07 Kcal/mol, Acetonitrile = -13.76 Kcal/mol, Aniline = -9.86 Kcal/mol, Benzene = -6.73 Kcal/mol, CCl₄ = -8.29 Kcal/mol, Chlorobenzene = -6.02 Kcal/mol, Chloroform = -12.97 Kcal/mol, Cyclohexane = -18.67 kcal/mol, Dichloroethane = -17.77 Kcal/mol, Diethylether = -15.99 Kcal/mol, DMSO = -19.50 Kcal/mol, Ethanol = -38.77 Kcal/mol, Isoquinoline = 725.89 Kcal/mol, Methanol = -39.77 Kcal/mol, Nitromethane = -12.28 Kcal/mol, Quinoline = 726.41 Kcal/mol, THF = -15.41 Kcal/mol, Toluene = -16.96 Kcal/mol, and Water = -36.41 Kcal/mol. These values could be an indication that the studied molecule will be mostly soluble in ethanol, methanol and water, and this can be related to the results obtained for the dipole moment and polarizability. Indeed, the calculated results indicate that morin flavonoid will be more soluble in polar solvents and insoluble in quinoline and isoquinoline. The large solubility in water implies that this molecule could be useful in water cleaning because it easily forms complexes with heavy metal atoms.

The HOMO and LUMO of the flavonoid morin calculated with the M05-2X/6-31+G(d,p) model chemistry are displayed in Fig. 3. The reactive sites can be identified through an

Table 2 Electronic transition states of the Pt(II)-morin complex (nm, eV, oscillator strengths (f), and transition assignments as calculated with TD-DFT and the M05-2X/LANL2DZ level of theory

Number	nm	eV	(f)	Assignment; H = HOMO, L = LUMO
1	396.7	3.13	0.0045	S H-3 → L+6(9%) H-5 → L+6(+8%)
2	389.1	3.19	0.2157	S H-0 → L+0(+65%)
3	370.9	3.34	0.0138	S H-4 → L+6(+18%) H-5 → L+6(+8%) S H-4 → L+11(6%)
4	366.0	3.39	0.0789	S H-0 → L+0(+13%) H-3 → L+6(+10%) S H-2 → L+6(+5%)
5	355.7	3.49	0.0049	S H-7 → L+6(17%) H-7 → L+11(+7%) S H-5 → L+6(6%)
6	334.4	3.71	0.3984	S H-1 → L+1(+72%) H-0 → L+1(6%)

Table 3 Electronic transition states of the Pd(II)-morin complex (nm, eV, oscillator strengths (f), and transition assignments as calculated with TD-DFT and the M05-2X/LANL2DZ level of theory

Number	nm	eV	(f)	Assignment; H = HOMO, L = LUMO
1	486.4	2.55	0.0016	S H-5→L+4(+21%) H-5→L+3(+16%)
2	465.4	2.66	0.0038	S H-12→L+4(7%) H-2→L+4(+6%) S H-12→L+3(6%)
3	450.1	2.75	0.0011	S H-7→L+4(14%) H-7→L+3(11%) S H-8→L+4(9%) H-8→L+3(7%)
4	428.8	2.89	0.0029	S H-11→L+4(+11%) H-9→L+4(+9%) S H-11→L+3(+9%) H-9→L+3(+7%)
5	382.3	3.24	0.2988	S H-0→L+0(+81%)
6	334.7	3.70	0.3842	S H-1→L+1(+74%) H-0→L+1(6%)

analysis of the total and orbital densities. The representation of the calculated HOMO and LUMO densities in Fig. 3 show that the electrophilic attack would occur preferentially at O15 and the nucleophilic attack at C1 and C4 atoms.

Within the conceptual framework of DFT [12], the chemical potential μ , which measures the escaping tendency of electron from equilibrium is defined as:

$$\mu = \left(\frac{\partial E}{\partial N} \right)_{v(r)} = -\chi, \quad (1)$$

where χ is the electronegativity.

The global hardness η can be seen as the resistance to charge transfer:

$$\eta = \frac{1}{2} \left(\frac{\partial^2 E}{\partial N^2} \right)_{v(r)}. \quad (2)$$

Using a finite difference approximation and Koopmans' theorem [14–17], the above expressions can be written as:

$$\mu \approx -\frac{1}{2}(I + A) \approx \frac{1}{2}(\varepsilon_{L+} + \varepsilon_H) \quad (3)$$

$$\eta \approx -\frac{1}{2}(I - A) \approx \frac{1}{2}(\varepsilon_{L-} - \varepsilon_H) \quad (4)$$

where ε_H and ε_L are the energies of the highest occupied and the lowest unoccupied molecular orbitals, HOMO and LUMO, respectively.

Table 4 Electronic transition states of the Zn(II)-morin complex (nm, eV, oscillator strengths (f), and transition assignments as calculated with TD-DFT and the M05-2X/LANL2DZ level of theory

Number	nm	eV	(f)	Assignment; H = HOMO, L = LUMO
1	406.7	3.05	0.3844	S H-0→L+0(+84%)
2	331.9	3.74	0.4990	S H-1→L+1(+77%) H-1→L+0(6%)
3	313.2	3.96	0.1421	S H-2→L+0(+73%)
4	309.9	4.00	0.0074	S H-0→L+1(+87%)
5	308.5	4.02	0.0010	S H-12→L+1(+60%) H-14→L+1(+7%) S H-0→L+1(6%)
6	298.5	4.15	0.0042	S H-1→L+0(+85%) H-1→L+1(+6%) S H-2→L+0(+5%)

The electrophilicity index ω represents the stabilization energy of the systems when it gets saturated by electrons coming from the surrounding:

$$\omega = \frac{\mu^2}{2\eta} \approx \frac{(I + A)^2}{2(I + A)} \approx \frac{(\varepsilon_{L+} + \varepsilon_H)^2}{2(\varepsilon_{L-} - \varepsilon_H)} \quad (5)$$

The validity of the Koopmans' theorem within the DFT approximation is controversial. However, it has been shown [28] that although the KS orbitals may differ in shape and energy from the HF orbitals, the combination of them produces conceptual DFT reactivity descriptors that correlate quite well with the reactivity descriptors obtained through Hartree-Fock calculations. Thus, it is worth calculating the electronegativity, global hardness and global electrophilicity for the flavonoid morin and the Pt(II), Pd(II) and Zn(II) complexes using both approximations in order to verify the quality of the procedures.

The results for the vertical I and A of the morin, Pt(II)-morin, Pd(II)-morin, and Zn(II)-morin molecules obtained through energy differences between the ionized and the neutral state, calculated at the geometry of the neutral molecule, the HOMO and LUMO energies, and the calculated values of the electronegativity, global hardness and global electrophilicity using the IP and A, and using the HOMO and LUMO energies, within the Koopmans' theorem, are displayed in Table 6.

Table 5 Total energy E, dipole moment μ , polarizability α , calculated with the M05-2X/6-31+G(d,p) and the M05-2X/LANL2DZ levels of theory

Molecule	E (a.u.)	μ (Debye)	α (Bohr ³)
Morin	-1104.101	7.99	98.70
Pt(II)-morin	-2478.206	16.65	156.08
Pd(II)-morin	-2485.798	17.28	158.12
Zn(II)-morin	-2505.403	15.28	193.91

The agreement between the results of both groups of conceptual DFT reactivity descriptors is qualitatively correct for the four molecules, having very good results for the bare morin molecule. The ionization potentials I are better described using the Koopmans' theorem approximation than the electron affinities A, and this can be ascribed as the main source of discrepancies.

The condensed Fukui functions can also be employed to determine the reactivity of each atom in the molecule. The corresponding condensed functions are given by $f_k^+ = q_k(N+1) - q_k(N)$ (for nucleophilic attack), $f_k^- = q_k(N) - q_k(N-1)$ (for electrophilic attack), and $f_k^0 = [q_k(N+1) - q_k(N-1)]/2$ (for radical attack), where q_k is the gross charge of atom k in the molecule.

It is possible to evaluate condensed Fukui functions from single-points calculations directly, without resorting to additional calculations involving the systems with N-1 and N+1 electrons:

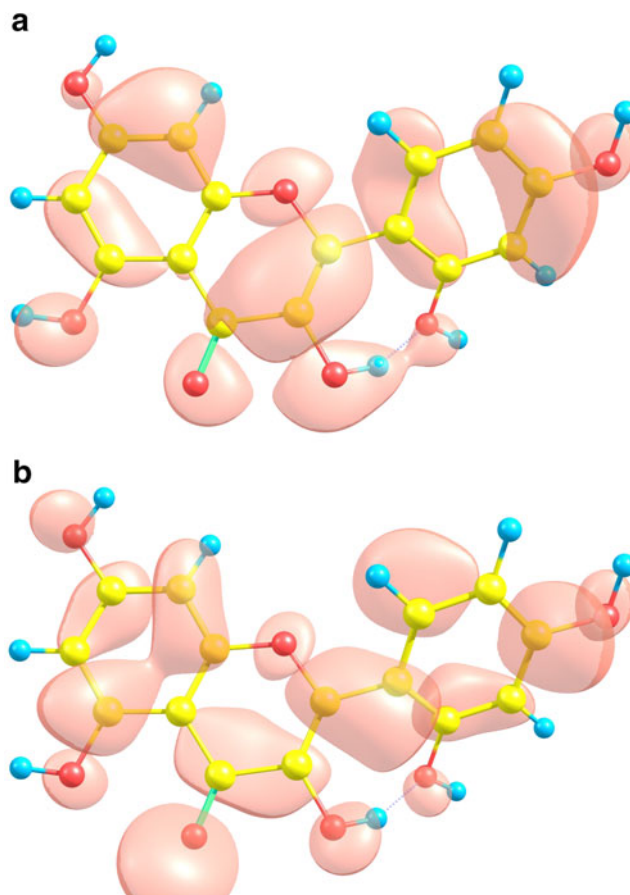
$$f_k^+ = \sum_{a \in k} \left[c_{ai}^2 + c_{ai} \sum_{b \neq a} c_{bi} S_{ab} \right] \quad (\text{where } i = \text{LUMO})$$

and

$$f_k^- = \sum_{a \in k} \left[c_{ai}^2 + c_{ai} \sum_{b \neq a} c_{bi} S_{ab} \right] \quad (\text{where } i = \text{HOMO})$$

Table 6 Ionization potential I, electron affinity A, HOMO energy, LUMO energy, electronegativity, global hardness and global electrophilicity of morin, Pt(II)-morin, Pd(II)-morin, and Zn(II)-morin calculated with the M05-2X/6-31+G(d,p) and M05-2X/LANL2DZ levels of theory, and Eqs. 3, 4 and 5. The first group of conceptual DFT reactivity descriptors corresponds to calculations based on energy differences, while the second group belongs to results based on HOMO and LUMO energies

Molecule	Morin	Pt(II)-morin	Pd(II)-morin	Zn(II)-morin
I (eV)	7.274	7.670	7.672	7.307
A (eV)	0.109	1.616	1.613	1.452
ϵ HOMO (eV)	-7.166	-7.238	-7.241	-6.789
ϵ LUMO (eV)	-0.684	-2.103	-2.100	-1.896
χ (eV)	3.917	4.643	4.643	4.380
η (eV)	3.808	3.027	3.030	2.928
ω (eV)	2.015	3.561	3.557	3.276
χ (eV)	3.925	4.671	4.671	4.343
η (eV)	3.241	2.568	2.571	2.447
ω (eV)	2.377	4.248	4.243	3.854

**Fig. 3** HOMO and LUMO of the morin flavonoid calculated with the M05-2X/6-31+G(d,p) model chemistry

with c_{ai} being the LCAO coefficients and S_{ab} the overlap matrix. The condensed Fukui functions are normalized, thus $\sum_k f_k = 1$ and $f_k^0 = [f_k^+ + f_k^-]/2$.

The sites for electrophilic attack will be those atoms bearing a negative charge and where the Fukui function f_k^- is a maximum, while the sites for potential nucleophilic attack would depend on the values of f_k^+ on the atoms with a positive charge density.

The results from the calculation of the condensed Fukui functions for nucleophilic, electrophilic and radical attack have been obtained by resorting to the AOMix molecular analysis program [25] and are the C1, O15 and C1, respectively.

Conclusions

In this work, the molecular structure and properties of the flavonoid morin and its Pt(II), Pd(II) and Zn(II) complexes have been calculated using DFT through the M05-2X density functional and the 6-31+G(d,p) and LANL2DZ basis sets. Based on these structures, the IR spectra have been calculated, displayed, and the principal transitions have been explained. The UV-Vis of each molecule has been calculated with the same density functional and a 6-31+G(d,p) basis set. All calculations have been performed in the presence of water as a solvent. Every spectrum has been described by detailing six excited states, and the HOMO-LUMO transitions have been identified.

Some electronic properties like the total energy E , the dipole moment μ and the isotropic polarizability α have also been calculated, with the pKa of the most acidic hydrogen in each having been determined through a procedure implement in MOPAC 2009. This could be of importance to understand the ability of this flavonoid to complex heavy metals for the cleaning of water.

A comparison between the ionization potential I and electron affinity A of the four systems calculated through two different procedures has been assessed in order to validate them. It could be concluded that, at least for the systems under study, the conceptual DFT reactivity parameters calculated directly from the HOMO and LUMO of the ground state of the morin flavonoid and the metallic complexes constitute a valid alternative to the values derived from the vertical I and A .

The HOMO and LUMO of each carotenoid have been used as a means of determining the reactivity of them, and the nucleophilic, electrophilic and radical active sites have been identified with the aid of the calculation of condensed Fukui functions.

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