

E-ISSN: 2709-9423

P-ISSN: 2709-9415

JRC 2023; 4(1): 39-46

© 2023 JRC

www.chemistryjournal.net

Received: 12-11-2022

Accepted: 18-12-2022

R Chabi Doco

Laboratory of Theoretical Chemistry and Molecular Spectroscopy (LACTHESMO), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi (UAC); 03 BP 3409 Cotonou, Benin

MTA Kpota Houngue

Laboratory of Theoretical Chemistry and Molecular Spectroscopy (LACTHESMO), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi (UAC); 03 BP 3409 Cotonou, Benin

Urbain A Kuevi

Laboratory of Theoretical Chemistry and Molecular Spectroscopy (LACTHESMO), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi (UAC); 03 BP 3409 Cotonou, Benin

YGS Atohoun

Laboratory of Theoretical Chemistry and Molecular Spectroscopy (LACTHESMO), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi (UAC); 03 BP 3409 Cotonou, Benin

Correspondence**R Chabi Doco**

Laboratory of Theoretical Chemistry and Molecular Spectroscopy (LACTHESMO), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi (UAC); 03 BP 3409 Cotonou, Benin

Physicochemical modeling of myricetin complexes by Zinc II ions

R Chabi Doco, MTA Kpota Houngue, Urbain A Kuevi and YGS Atohoun

Abstract

Myricetin is phenolic compound, commonly found in vegetable kingdom (fruits, vegetables, roots etc.) and an integral part of daily diet of humans. Several experimental and theoretical works have shown that this molecule has an important antioxidant power.

Indeed, since the discovery of relationship between antioxidant activity of certain phenolic compounds and their ability to chelate metal ions, many experimental studies devoted to complexation of molecules such as quercetin, myricetin, kaempferol, rutin, morine with various metals (Cobalt, Nickel, Zinc, Copper, Molybdenum, Europium) were realized. However, these experimental studies do not yet constitute a standard means of determining complexation sites of molecules.

In present work, study of complexation of myricetin by Zn^{2+} ion was carried out by Hatree-Fock method, and in 6-311G (d, p) base set. The results of various calculations made it possible to:

- release hydroxyl groups as myricetin complexation sites;
- note that the complexes obtained are more antioxidants than myricetin;
- show that the complexation of myricetin causes bathochromic shifts of absorption bands.

Keywords: Hatree-fock, myricetin, complexe, antioxidant

Introduction

The ability of phenolic compounds to form complexes with metals (Iron, Magnesium, Aluminum, Copper, Zinc.) by process of chelation has long been used for analytical purposes, especially for revelation of chromatograms and for determination of these substances (Crichton *et al.*, 2001) [2]. Today, thanks to their complexing properties, flavonoids are used to detect the presence of metal ions such as iron, Zirconium, Antimony (Pierre and *al.*, 2002) [15]. It has long been known that phenomenon of complexation plays the most important role in the coloration of plants and, studies have shown that the ability of flavonoids to inhibit the growth and development of certain insects stem from their complexing properties (Tapiero and *et al.*, 2001) [18].

Antioxidant activity of flavonoids is related to this ability to complex metals. These molecules can trap free radicals responsible for oxidation by complexing catalyst metal ions of the formation reaction of these radicals (Ke & Qian, 2003) [11]. Indeed, since the discovery of relationship between activity of certain flavonoids and their ability to chelate metal ions, many studies are devoted to complexation of molecules such as quercetin, rutin, morine with various metals, Cobalt, Nickel, Copper, Molybdenum, Europium (Chaves and *et al.*, 2007) [3] have been realized.

Several theoretical and experimental work on flavonoid coordination properties have been published in literature and often contradictory results have been obtained with regard to metal/ligand binding site.

Experimentally, for example, studies have shown that these contradictions are due to the variation of conditions in study environments. Indeed, it is generally accepted that in alkaline solutions, the Fe^{3+} , Cu^{2+} , Zn^{2+} and Al^{3+} ions have the highest affinity for ortho-dihydroxyl group of quercetin (Y. Hara and *al.*, 2001, Maria M. Kasprzak *et al.*, 2005) [20, 25]. The study in acid solution of different chelation sites of quercetin in the presence of iron has shown that catechol group remains the main chelation site of Fe (J. Cui and *et al.*, 2013) [9]. In the same year, Dimitric Markovic and *al.* presented data that corroborated opposite (Y. Hara, 2001) [20]. They reported the formation of Fe-quercetin complex in an acidic solution, with coordination via sites 3-4 or 4-5 (Figure 1), whereas for a high pH solution, the binding of Fe

to the catechol group was advocated. For different solvents used for fisetin, these same authors also observed the formation of a fisetin-Fe complex involving coordination via the 3-4 site. The reduction of Fe^{3+} to Fe^{2+} by fisetin at acidic pH has also been described, while at higher pH, Fe^{3+} and Fe^{2+} complexes coexist.

On theoretical side, several authors using DFT methods have shown that Cr^{3+} ions promote the deprotonation of the 4-5 sites of quercetin and luteolin (Maria M. Kasprzak *et al.*, 2005, Jun Ren and *et al.*, 2007).^[21, 25], whereas Pb^{2+} ions bind preferentially to the 3'-4 site of each of these molecules (Katiyar Santosh K, *et al.*, 2008)^[22]. Other theoretical studies published in the literature have reached the same conclusions (M. Leopoldini and *al.*, 2006)^[12]. Also in 2012, Y. Zhang and *al.* performed a DFT study on quercetin complexes with aluminum. They indicated that there is difference between chelation sites of the solid state and those in solution. For their part, in 2013 by the DFT/B3LYP/6-31G method (2df, 3dp), by studying the UV-vis and IR spectra of luteolin complexes with Cadmium II, SONG Liao and *al.* Have shown that the chelation sites of this molecule are those of catechol par.

Of all foregoing, it should be noted that to our knowledge, no theoretical work with respect to the chelation sites of myricetin by Zn^{2+} has yet been performed. Indeed, several experimental works (Ez-zohra NKHILI; thesis 2009)^[5] and theoretical (Chabi and *al.*, 2018)^[23] have shown that this molecule has very important antioxidant power.

The objective of the present work is to determine the best antioxidant among the complexes of the myricetin by methods of quantum chemistry. The reactivities of different chelation sites will be compared with each other, in order to deduce the preferential sites for reinforcing antioxidant capacities of this molecule. To achieve this objective, various electronic and spectroscopic parameters will be calculated and the results will allow to deduce a ranking order of the antioxidant powers of each complexes as well as the most appropriate chelation sites for this molecule.

Materials and Methodology

Materials

Chemical systems in our study were myricetin and complexes obtained from myricetin and the Zn^{2+} ion provided by zinc chloride (ZnCl_2)

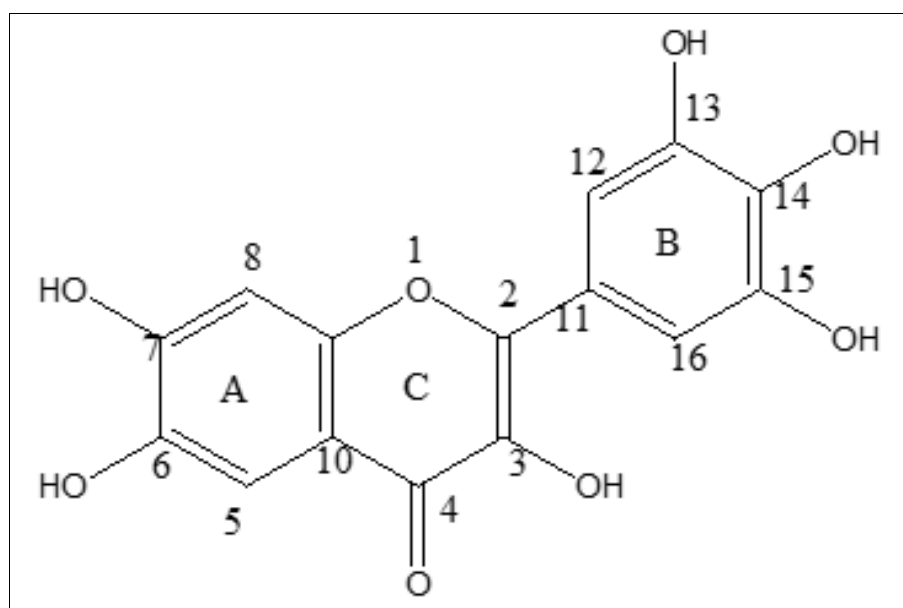


Fig 1: Représentation spatiale de la myricétine

Methodology

For myricetin and each complex, calculated parameters were:

Structural parameters

For molecule with several degrees of freedom, potential energy surface is hyper-surface with several minima and maxima. The maxima correspond to transition states and the minima to equilibrium geometries or conformations of molecule. In a state of minimal energy, vibration frequencies of molecule are all positive. The lowest of minima called global minimum, represents the most stable conformation of studied system.

Each of compound was studied by Hatree-Fock method in the 6-311G (d, p) atomic orbital base. At the beginning of the complexation process, ZnCl_2 molecule was placed about 2,50 Å of each of hydroxyl groups considered.

Electronic parameters

$$Gap_{(HOMO-LUMO)} = ELUMO - EHOMO,$$

which is weaker as molecule has a high antioxidant power

- **Hardness (η)** which expresses the resistance of molecule to the change of its number of electrons or to charge transfer (Bonin KD and *al.*, 1997). The harder the hardness, less reactive the molecule is:

$$\eta = \frac{(ELUMO - EHOMO)}{2}$$

- **Electronegativity (χ)**, which measures tendency of chemical species to attract electrons (Morrel H., 2006)^[13].

$$\chi = - \frac{(\text{ELUMO} + \text{EHOMO})}{2}$$

- **Electrophilic index (ω)**, which represents the stabilizing energy of molecule saturated by electrons from its surroundings (Payan-Gomez and *al.*, 2010):

$$\omega = \frac{\chi^2}{2\eta}$$

- **Electrofugacity**, which indicates the ability of a compound to donate one or more electrons $\Delta E_e = \omega + I$, $I = -\text{ELUMO}$ (Ayers and *al.*, 2005) [26]
- **Nucleofugacity** that reflects the ability of a compound to accept one or more electrons

$$\Delta E_n = \omega - A, A = -\text{EHOMO} \text{ (Ayers and } al., 2005) [26]$$

Spectroscopic parameters: such as Infra-red spectra and UV-visible spectra were calculated by TD-DFT method. This parameter will allow us to find the influence of complexation of myricetin on antioxidant properties of it. Calculations were made by Hatree-Fock method in the 6-311G (d, p) atomic orbital Pople base set (J.P. Perdew and *al.*, 1996) [24].

Results and Discussions

Study of structural properties of compound

Figures 2, 3, 4, 5 and 6 show optimized geometry of myricetin and each of the complexes obtained from myricetin and Zinc chloride (ZnCl_2). The various complexes obtained allow us to make following observations:

- For complex 1, there was formation of bond between O^{14} and Zn metal since the interatomic distance $\text{O}^{14}\text{Zn}^{34}$ is 1.98 Å, which is in agreement with experimental data

published in literature (Symonowicz *et al.*, 2012) [17]. The preferred complexation site is thus the O^{14} atom of the $\text{C}^8=\text{O}^{14}$ group. However, the geometry of the metal in the complex is trigonal rather than tetrahedral. This observation shows that the complex obtained is unstable.

- For complexes 2, 3 and 4, globally, hydroxyl groups $\text{O}^{26}\text{H}^{27}$ ($(\text{O}^{26} \text{-----} \text{Zn}^{34}) = 2.21 \text{ \AA}$) and $\text{O}^{24}\text{H}^{25}$ ($(\text{O}^{24} \text{-----} \text{Zn}^{34}) = 2.23 \text{ \AA}$), $\text{O}^{32}\text{H}^{33}$ ($(\text{O}^{30} \text{-----} \text{Zn}^{34}) = 2.20 \text{ \AA}$) and $\text{O}^{26}\text{H}^{27}$ ($(\text{O}^{30} \text{-----} \text{Zn}^{34}) = 2.21 \text{ \AA}$) of B cycle on one hand and $\text{O}^{30}\text{H}^{31}$ ($\text{O}^{30} \text{--- ---} \text{Zn}^{34}) = 2.12 \text{ \AA}$) of C cycle, on other hand are favorable to complexation of myricetin. Geometry of Zinc in these three complexes is tetrahedral which augurs a good complexation and therefore confirms that these hydroxyl sites are true sites of chelation of myricetin. This result is in agreement with experimental results published in literature (Jun Ren and *al.*, 2007, Symonowicz and *al.*, 2012) [21, 17]. According to these authors, the hydroxyl groups of the catechol part favor the chelation of flavonoids by metal ions.

From these analyzes, it appears that Zinc metal complexes can be obtained from myricetin. However, these results should be compared by calculating the electronic parameters of each of the complexes and myricetin in order to refine the conclusions of the present work.

Analysis of electronic parameters of myricetin and its complexes

For different complexes and myricetin, calculated values of electronic parameters, at Hatree-Fock levels approximation are recorded in table 1:

Table 1: Calculated Values (kJ/mol) of Electronic parameters of Complexes 1, Complex 2, Complex 3, Complex 4 and Myricetin

	E_{HOMO} (kJ/mol)	E_{LUMO} (kJ/mol)	E_{Gap} (kJ/mol)	ω (kJ/mol)	ΔE_e (kJ/mol)	ΔE_n (kJ/mol)
Myricétine	-831.25	157.5	988.75	105	656.25	1023.75
Complexe 1	-866.4	26.25	892.65	5773.36	5198.75	13098.75
Complexe 2	-866.4	78.76	945.16	3491.25	4672.5	2598.75
Complexe 3	-866.4	78.76	945.16	3491.25	4672.5	2598.75
Complexe 4	-787.65	105.02	892.67	5771.36	5196.75	13098.75

Results in Table 1 show that

- All of the four complexes gave, on the one hand, Gap (HOMO-LUMO) lower than of myricetin and on the other hand electrophilic index (ω) values higher than that of myricetin. These series of results, in agreement with experimental data published in literature, mean that the complexes are very stable and therefore more antioxidant than myricetin (CHERRAK Sabri Ahmed, Thesis 2017) [4]. Zinc II ion would then enhance antioxidant capacity of myricetin. Overall, the ranking order of the Gaps of the four complexes would be: Complex 1 < complex 4 < complex 2 \approx complex 3. Antioxidant activity of complexes 1 and 4 would therefore be greater than that of complexes 2 and 3.
- Of the four complexes, the highest values of electrofugacity (ΔE_e), nucleofugacity (ΔE_n) and electrophile index (ω) were obtained by complexes 1 and 4. This result indicates that these complexes are more antioxidants than complexes 2 and 3.

These analyzes show that complexes resulting from the chelation of myricetin with Zn II ion are more antioxidant than myricetin. Also, complexes 1 and 4 possess the highest antioxidant powers of the four complexes

Representation of HOMO-LUMO energies and iso surface of myricetin and each complex

For myricetin and each of the complexes 1, 2, 3 and 4, energies HOMO, LUMO and iso surface have been represented in figure 2, 3, 4, 5 and 6.

Analysis of these different figures reveals that:

- For myricetin, HOMO and LUMO are distributed along all three cycles (A, B and C), whereas for all four complexes these orbitals are distributed over the cycles (B and C). This result indicates that presence of Zn II ion modifies the distribution of electron cloud at level of myricetin; this promotes a high electron density at these two cycles. This implies an increase in antioxidant power.

- The representation of potential energy surface of each of complexes, shows globally, that areas of high electron density are at C^8O^{14} , $O^{26}H^{27}$, $O^{24}H^{25}$, $O^{32}H^{33}$, $O^{26}H^{27}$ and $O^{30}H^{31}$ groups. This distribution of electron density, due to the presence of Zn II ion made it possible to draw the same conclusions as above. The sites favorable for complexation of myricetin by Zn II ion are Oxygene (O) atom of C^8O^{14} , $O^{26}H^{27}$, $O^{24}H^{25}$, $O^{32}H^{33}$, $O^{26}H^{27}$ and $O^{30}H^{31}$ groups.

Influence of complexation on UV-vis spectra of myricetin

The absorption curves of UV-Visible spectrum of myricetin and complexes 1, 2, 3, 4 were calculated and represented at HF/6-311G (d, p) level (Figure 6). From analysis of different absorption curves it follows that:

- Complex 1, has five (05) UV-screw absorption peaks whose absorption waveband varies from 100 to 350 nm. With regard to complexes 2, 3 and 4, they have 4 peaks and absorption wavelengths are between 50 nm and 300 nm. On other hand, Myricetin has 4 absorption peaks less hypertrophied than those of the four complexes and the length of the absorption band is between 98nm and 300nm. From these analyzes, it appears that, the presence of Zn II ion, It has strengthened electronic delocalization of myricetin. This result indicates that each of the four complexes has broader range of UV-visible spectrum than myricetin. It follows that complexes 1, 2, 3 and 4 are more antioxidant than myricetin. the complex 1 having presented wider range of absorption band compared to other complexes, thus appears the most antioxidant of the 4 complexes. Indeed, according to the experimental work published in literature by Ez-zohra NKHILI in 2009 ^[5], molecules with wide range of UV-vis spectra facilitate electronic delocalisation and have a strong antioxidant character.
- Comparison between UV-visible absorption spectra of complexes revealed that of the four, complexes 2, 3 and 4 showed the same absorption curves with almost the same number of peaks. Which means that these complexes possess very close antioxidant powers.

From all above, it can be concluded that complexation of myricetin by Zinc II ions causes bathochromic displacements of the absorption bands of myricetin and increases antioxidant power thereof. This behavior is observed especially with complex 1.

Analysis of Infra-Red Spectra of Myricetin and Complexes 1, 2, 3 and 4

Infra Red (IR) spectra of myricetin and each of 4 complexes are shown in Figures 2, 3, 4,5 and 6 below. From analysis of different spectra, it appears that:

- Infra-red spectra of myricetin and its complexed forms are dominated by bands in spectral range 0-4.200 cm^{-1} .
- Significant frequency changes around the spectral band between 4000 cm^{-1} and 4250 cm^{-1} are observed between the IR spectra of myricetin and that of the complexes. This observation between IR spectra indicates that chelation causes very important structural variations in myricetin. This result is in agreement with the experimental results published by Laurence VRIEL YNCK in 1996.
- IR spectra of complexes 1, 2, 3 and 4 gave less intense

bands than those of myricetin. This result indicates that electronic offshoring is more important at level of complexes than myricetin. This implies a weakening of the hydroxyl (OH) bonds at the level of each of the complexes. Complexes 1, 2, 3 and 4 therefore appear to be more stable than myricetin. The Zn II ion strengthens the antioxidant power of myricetin.

- IR bands from 0 to 2000 cm^{-1} are virtually identical for myricetin and each of 4 complexes. On other hand, for band at 4000 cm^{-1} and 4250 cm^{-1} , we have difference between different peaks observed. By comparing this spectral band for the ligand (myricetin), and complexes 1, 2, 3 and 4, it is found that complexation peaks are obtained practically at level of band at 4150 cm^{-1} . These peaks corresponding to peak of the coordination link.

From these results, it follows that Zinc II ion modifies structural properties and increases the antioxidant activity of myricetin

The structure of Zinc in Complex 1 has a trigonal geometry. However, this complex has good antioxidant power. It therefore seems interesting to seek and find tetrahedral form by stabilizing it with other ligands for more judicious comparison of antioxidant properties.

Stabilisation of complex 1

Figure 7 shows the complex obtained from Zinc chloride ($ZnCl_2$) and two molecules of myricetin. The distance between groups (C^8O^{14} , $O^{28}H^{29}$) and $ZnCl_2$ for optimization of geometry is 2.50 Å.

From analysis of results, it appears that:

- Zinc metal structure is tetrahedral in complex (v). This result indicates that ZnII metal complex stabilizes with two molecules of myricetin. The distances (O---Zn) obtained on either side of two ligands being identical and is equal to 2.01 Å, justifies good coordination between Zn II and all the two molecules of myricetin.
- HOMO, LUMO orbitals are distributed along all three cycles (A, B and C) of the ligands. Similarly, the representation of potential energy surface of complex, shows that globally, areas of high electron density are at C^8O^{14} , $O^{26}H^{27}$, $O^{24}H^{25}$, $O^{32}H^{33}$, $O^{26}H^{27}$ and $O^{30}H^{31}$ (w) groups of this same ligand. around Zn II. This result, identical to that of complex 1, indicates that presence of Zn II ion modifies distribution of electron cloud at the level of myricetin and promotes a strong electronic delocalization at these cycles A, B and C.
- With regard to UV-vis and Infra-red spectra, the results obtained practically coincide with those of complexes 2, 3 and 4, with the difference that UV-vis spectrum of the complex has an absorption band varying from 124 nm to 325 nm. This means that the latter has slightly higher antioxidant power than that of 2,3 and 4 complexes.
- Calculation of energy Gap for the complex 5 gives 866.41 kJ/mol. This value being higher than those of complexes 1, 2, 3 and 4, indicates that the complex 5 would be more antioxidant. This result shows that the formation of complex from two molecules of myricetin further enhances more antioxidant capacity of the latter.

From these results, we can conclude that complex obtained from two molecules of myricetin is much more stable and therefore more antioxidant than complexes formed from a molecule of myricetin.

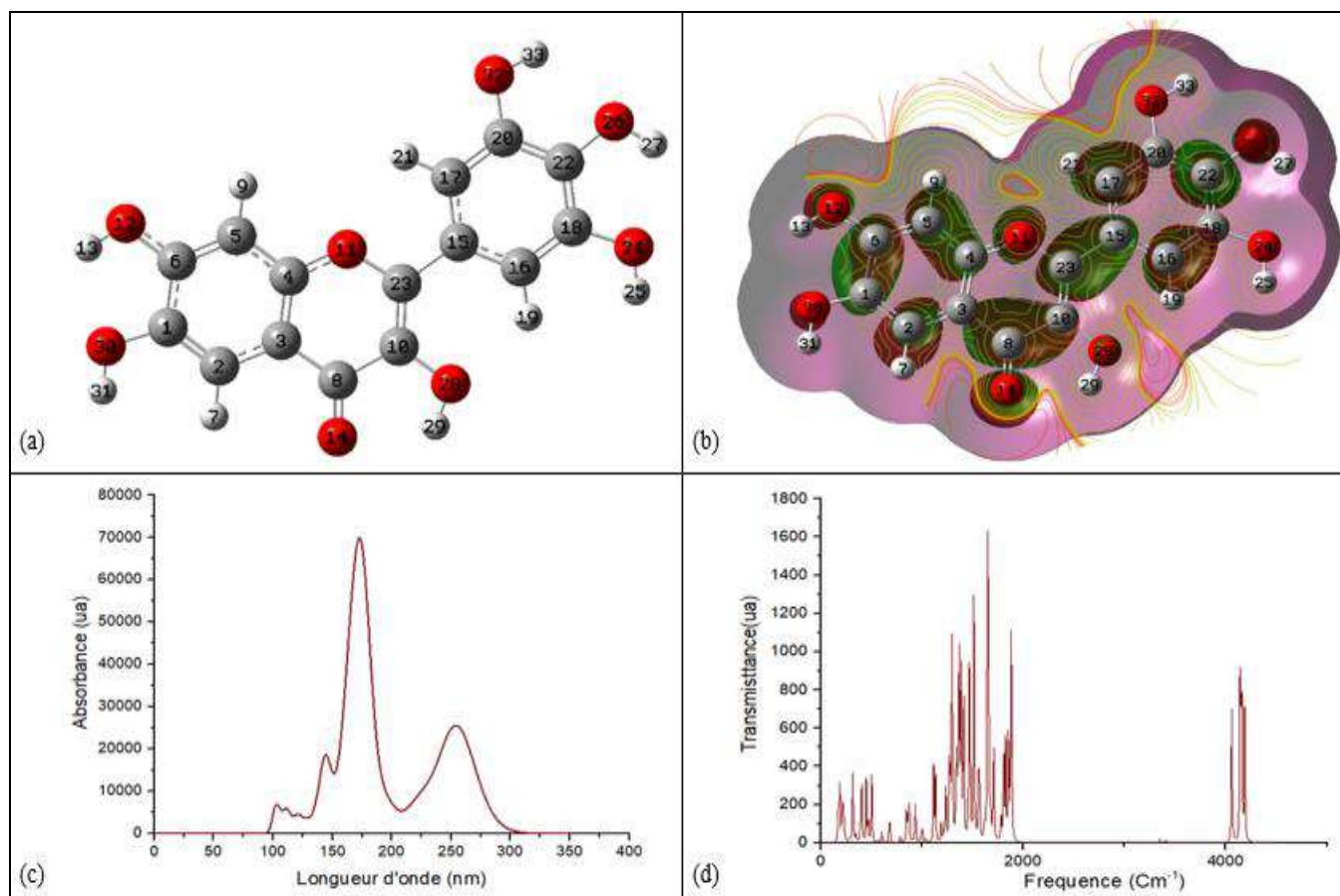


Fig 2: representation of optimized forms (a), HOMO and LUMO and SEP (b) orbitals, UV-vis (c) and IR (d) spectra of myricetin to HF / 6-311G (d, p)s

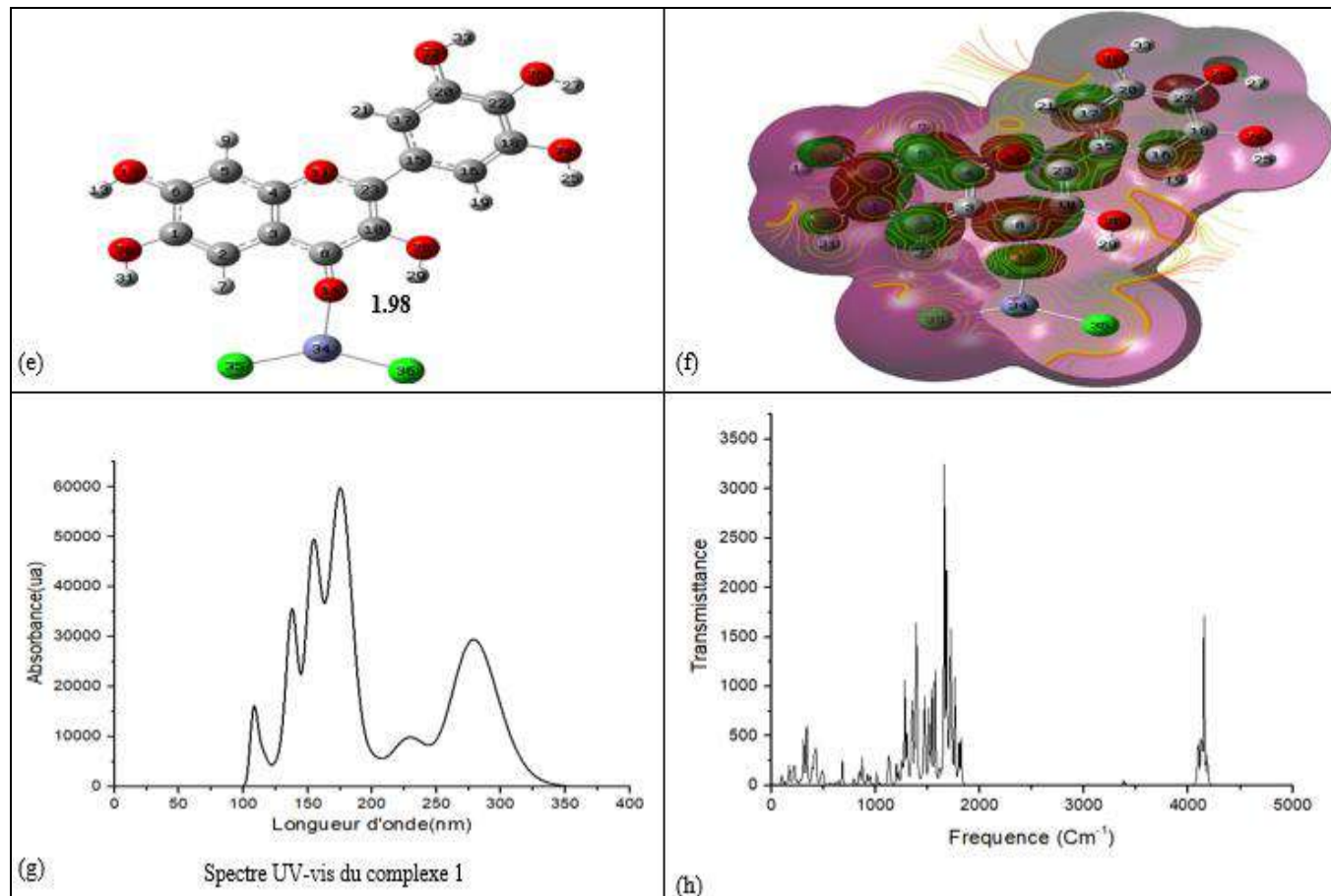


Fig 3: Representation of optimized forms (e), HOMO and LUMO and SEP (f) orbitals, UV-vis (g) and IR (h) spectra of complex 1 to HF / 6-311G (d, p)s

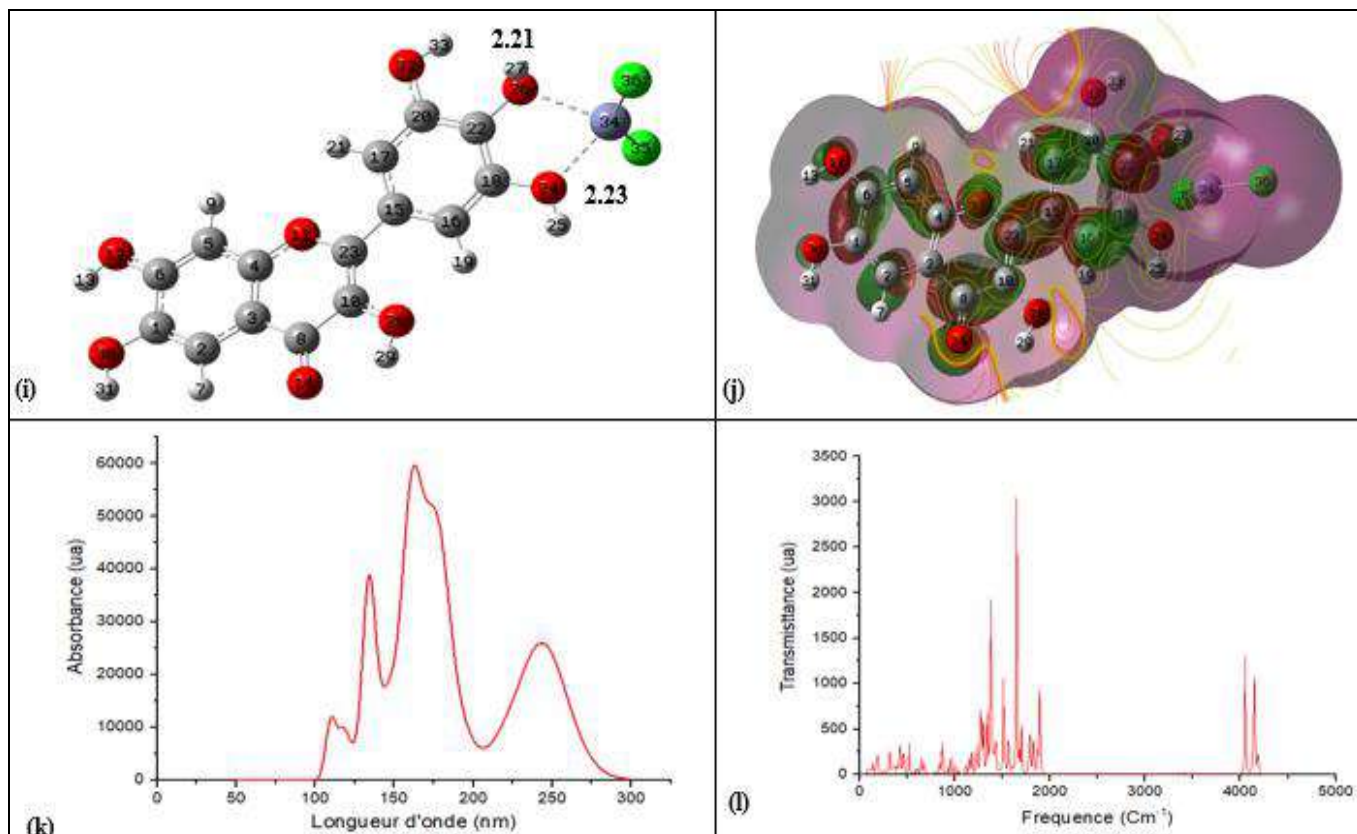


Fig 4: Representation of optimized forms (i), HOMO and LUMO orbitals, SEP (j), UV-vis (k) and IR (l) spectra of complex 2 to HF / 6-311G (d, p)

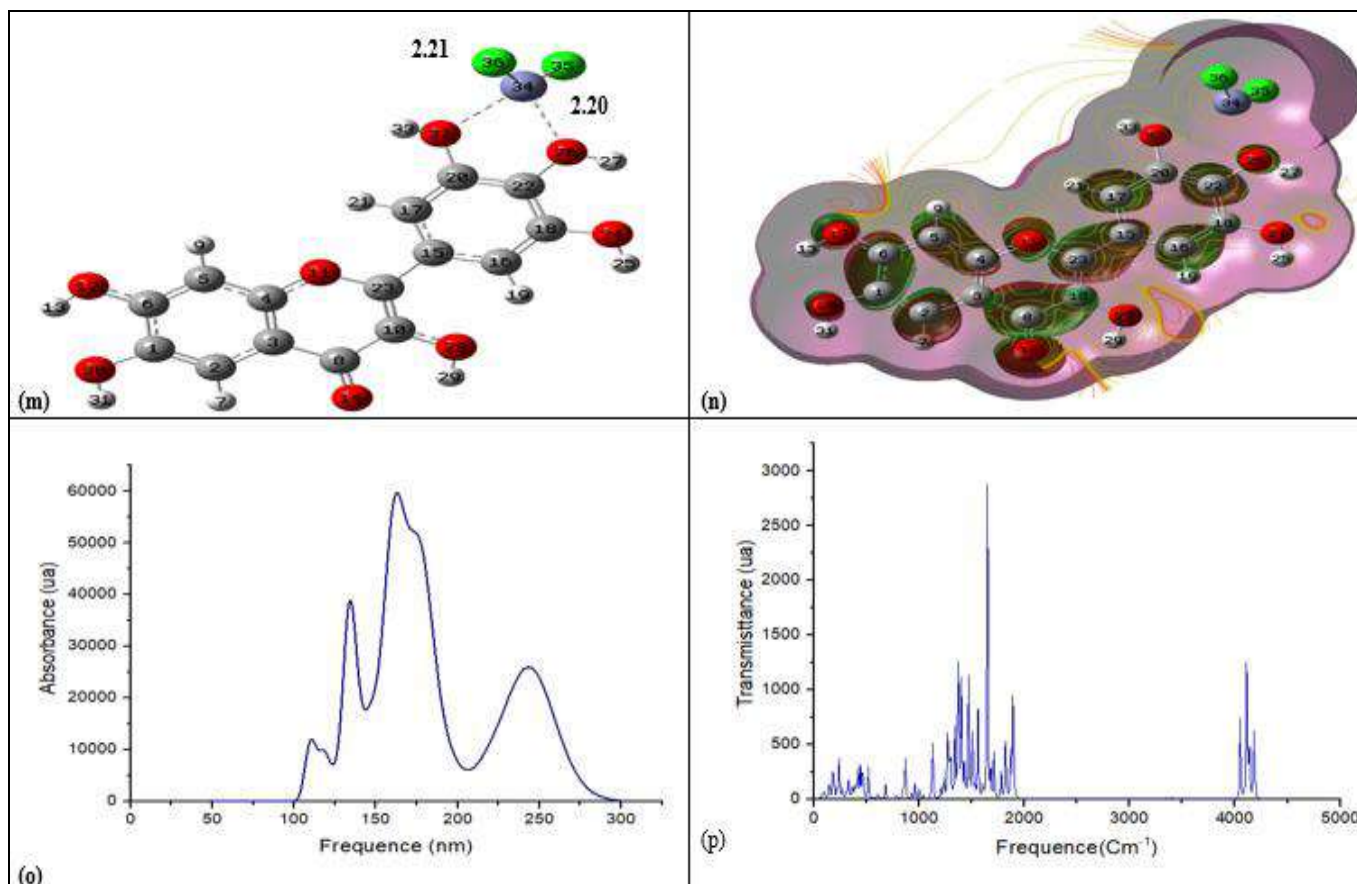


Fig 5: Representation of optimized forms (m), HOMO and LUMO orbitals, SEP (n), UV-vis (o) and IR (p) spectra of complex 3 to HF / 6-311G (d, p)

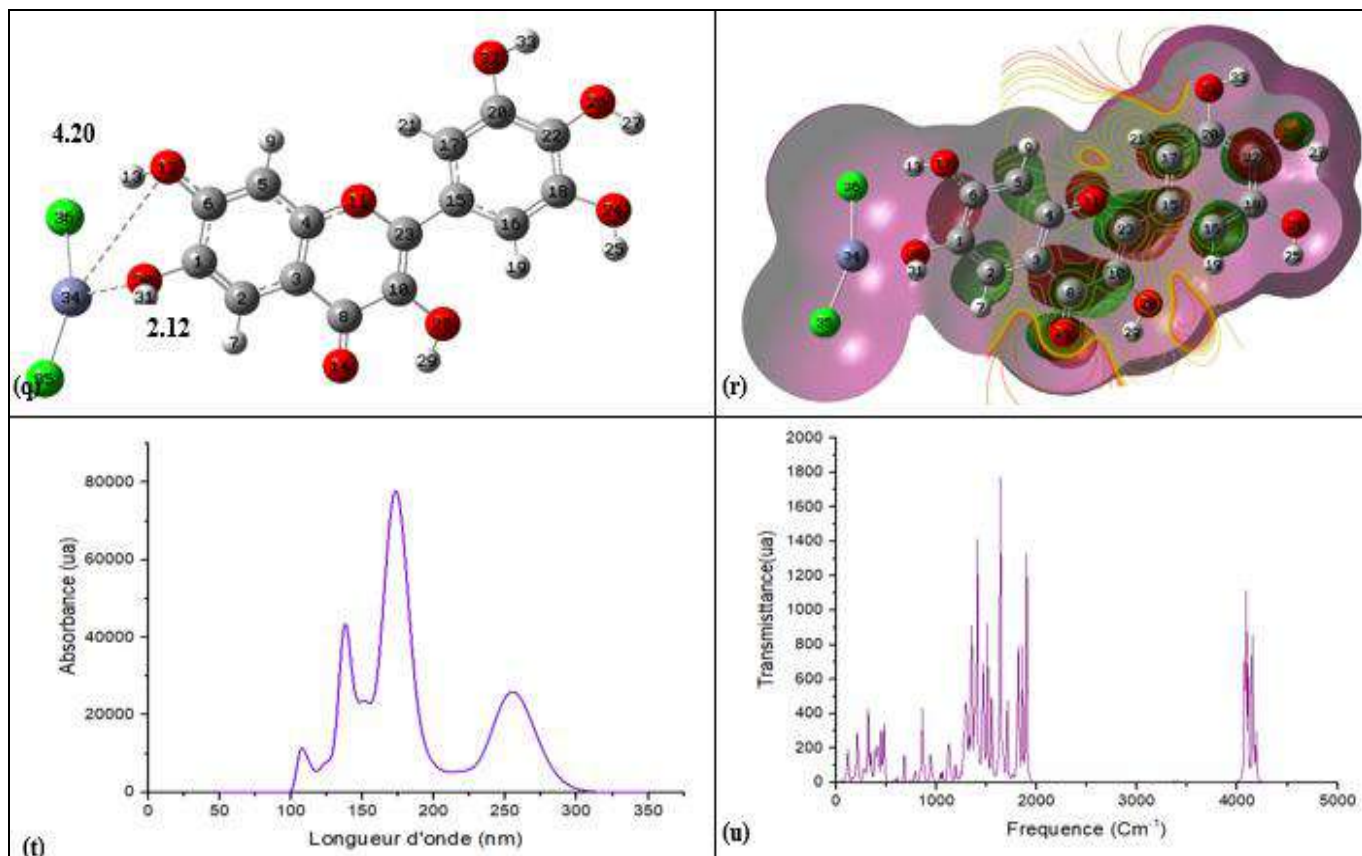


Fig 6: representation of optimized forms (q), HOMO and LUMO orbitals, SEP (r), UV-vis (t) and IR (u) spectra of complex 4 to HF / 6-311G (d, p)

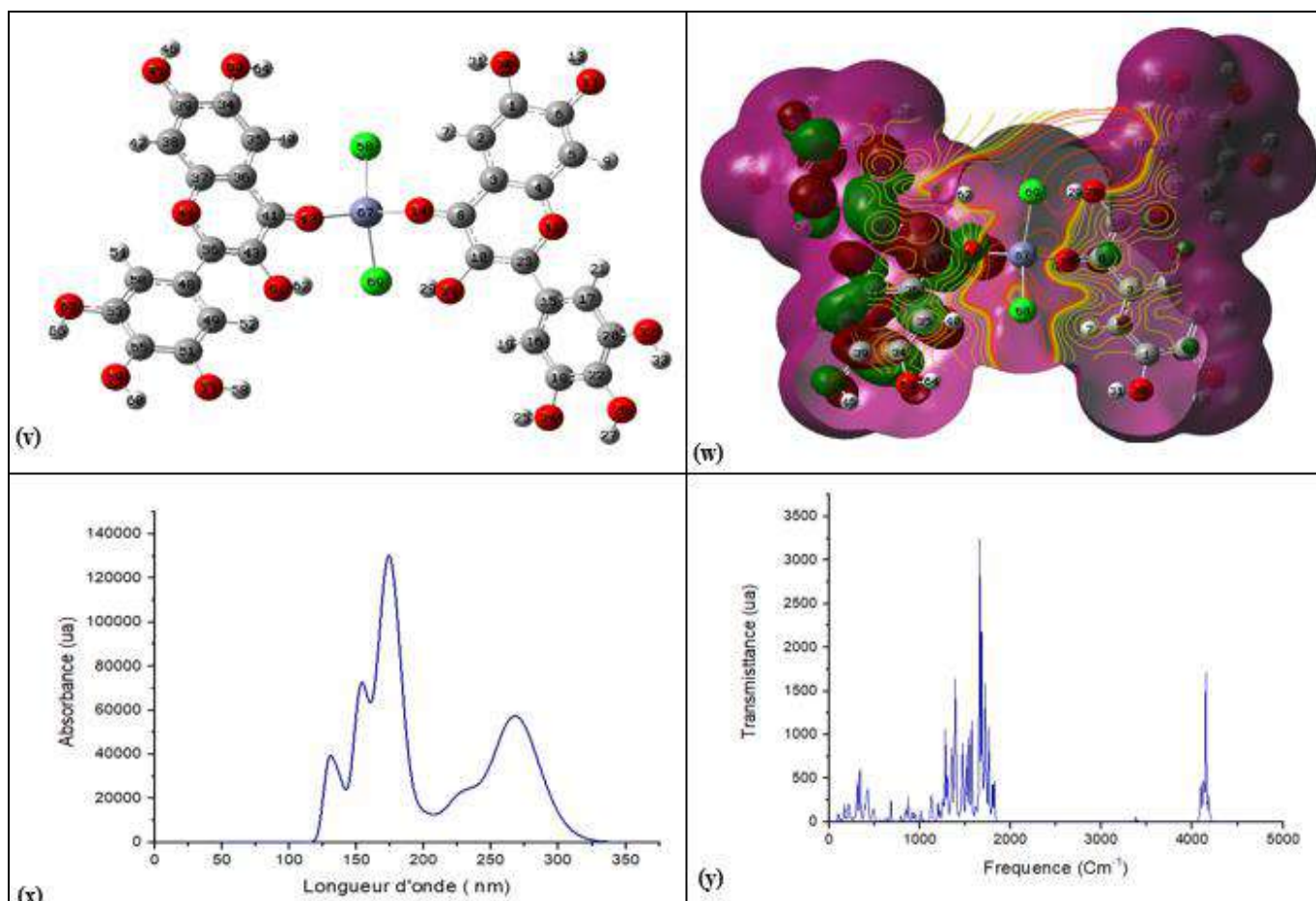


Fig 7: Representation of optimized forms (v), HOMO and LUMO orbitals, SEP (w), UV-vis (x) and IR (y) spectra of complex 5 to HF / 6-311G (d, p)

Conclusion

A theoretical study of chemical reactivities of myricetin and complexed forms was carried out by Hatree-Fock/6-311G (d, p) method. Comparison between calculated values of various structural, electronic and spectroscopic parameters allowed to:

- Release that oxygene (O) atoms of C⁸O¹⁴, O²⁶H²⁷, O²⁴H²⁵, O³²H³³, O²⁶H²⁷ and O³⁰H³¹ groups as complexing sites of myricetin
- note that complexes 1, 2, 3 and 4 from myricetin are more antioxidant than myricetin.
- show that complexes 1 and 4 are the most antioxidants of four complexes
- note that complexation of myricetin by Zinc II ions in some cases causes a bathochromic displacement of absorption bands of myricetin.
- show that complex obtained from two molecules of myricetin is more stable and therefore more antioxidant than the complexes formed from molecule of myricetin.

With regard to prediction of antioxidant properties of molecule and the complexes studied, theoretical results are in agreement with the experimental data published in the literature.

References

1. Ayers PW, Levy M. *Theor. chem, Acc.* 2000;103:353-360.
2. Crichton R, Pierre JL. *Old iron, young copper: from Mars to Venus. Biometals.* 2001;14(2):99-112.
3. Chaves FJ, Mansego ML, Blesa S, Gonzalez-Albert V, Jiménez J, Tormos MC, *et al.* Inadequate cytoplasmic antioxidant enzymes response contributes to the oxidative stress in human hypertension. *American journal of hypertension.* 2007;20(1):62-69.
4. Cherrak Sabri Ahmed. *Etude in vitro. de l'effet antioxydant des complexes Flavonoïdes –Métaux: Relation structure activité; Thèse; c2017.*
5. Ez-zohra Nkhili. *Polyphénols de l'alimentation: Extraction, Interactions avec les ions du Fer et du Cuivre, Oxydation et Pouvoir antioxydant; Thèse; c2009*
6. Payán G, Sergio A, Norma Flores H, Antonino P, Manuel, Piñón M, *et al.* Computational molecular characterization of the flavonoid rutin; *Chemistry Central Journal.* 2010;4:12.
7. Goitia MT, Montero M, Allan Bulletin. *de la Societé Quimica del Peru Fernandez Band, B.S. A.L; c1988,* 171.
8. Harborne JB. (ed.), Chapman and Hall, London, p. 399.
9. Cui J, Li S. Shaoshun, *Mini-Rev. Med. Chem., and refs therein M.* 2013;13:1357-1368.
10. Jun Ren, Sheng Meng, Ch. Lekka E, Efthimios Kaxiras. *Complexation of Flavonoids with Iron: Structure and Optical Signatures; J Phys. Chem. B.* 2008;112(6):1845-1850.
11. Ke Y, Qian ZM. *Iron misregulation in the brain: a primary cause of neurodegenerative disorders. The Lancet Neurology.* 2003;2(4):246-253.
12. Leopoldini N, Russo S, Chiodo, Toscano M. *J Agric. Food Chem.* 2006;54(17):6343-6351.
13. Morrel W. Cohen and Adam, *Journal of Statistical Physics, Hardness and Electronegativity Equalization in Chemical Reactivity Theory; H; c2006.*
14. Maria Kasprzak M. A Andrea Erxleben, Justyn Ochockia; *Properties and applications of flavonoid metal complexes; The Royal Society of Chemistry J Name.* 2013;00:1-3.
15. Pierre J, Fontecave M, Crichton R. *Chemistry for an essential biological process: the reduction of ferric iron. Bio metals.* 2002;15:341-346.
16. Song Xiao-Li, Gao Li-Geao, Gapo Wei. *Chelation between luteolin and Cd(II): spectroscopic studies and theoretical calculation, chinese journal of inorganic chemistry.* 1989-1992;29(9).
17. Symonowicz M, Kolanek M. *Flavonoids and their properties to form chelate complexes; c2012.*
18. Tapiero H, Gate L, Tew K. *Iron: deficiencies and requirements. Biomedicine & pharmacotherapy.* 2001;55(6):324-332.
19. Weirong Cai, Yong Chen, Liangli ang Xie, Hong Zhang, Chunyu uan Ho. *Characterization and density functional theory study of the antioxidant activity of quercetin and its sugar-containing analogues, Eur Food ResTechnol.* 2014;238:121-128.
20. Hara Y, Jovanovic SV, Steenken S, Simic MG. *J Chem. Soc. Perkin Trans.* 2001;2:2497-2504.
21. Ren J, Cheng W, Li S, Suckewer S. *A new method for generating ultraintense and ultrashort laser pulses. Nature Physics.* 2007 Oct;3(10):732-6.
22. Katiyar SK. *Grape seed proanthocyanidines and skin cancer prevention: inhibition of oxidative stress and protection of immune system. Molecular nutrition & food research.* 2008 Jun;52(S1):S71-6.
23. Chabi-Jesus C, Ramos-González PL, Tassi AD, Guerra-Peraza O, Kitajima EW, Harakava R, Beserra Jr JE, Salaroli RB, Freitas-Astúa J. *Identification and characterization of citrus chlorotic spot virus, a new dichorhavirus associated with citrus leprosis-like symptoms. Plant Disease.* 2018 Aug 17;102(8):1588-98.
24. Perdew JP, Burke K, Ernzerhof M. *Generalized gradient approximation made simple. Physical review letters.* 1996 Oct 28;77(18):3865.
25. Kasprzak MM, Erxleben A, Ochocki J. *Properties and applications of flavonoid metal complexes. Rsc Advances.* 2015;5(57):45853-77.
26. Effler PV, Pang L, Kitsutani P, Vorndam V, Nakata M, Ayers T, *et al.* *Dengue fever, hawaii, 2001–2002. Emerging infectious diseases.* 2005 May;11(5):742.