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ORIGINAL ARTICLE

Determination of phenolic compounds and antioxidant potential of aqueous extracts of *Curcuma longa* L., *Piper nigrum* L. and *Cuminum cyminum*: an experimental and a quantum-mechanical study

Determinação de compostos fenólicos e potencial antioxidante dos extratos aquosos de *Curcuma longa* L., *Piper nigrum* L. e *Cuminum cyminum*: um estudo experimental e quanto-mecânico.

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Abstract

Objectives: Evaluation of phenolic compounds and antioxidant activities of aqueous extracts of *C. longa*, *P. nigrum* and *C. cyminum*. In addition to proposing a quantum-mechanical model to evaluate the antioxidant activity. **Methods**: The aqueous extracts were prepared using roots of the *Curcuma longa* L., seeds of the *Piper nigrum L*. and seeds of *Cuminum cyminum*. The extracts were subjected to tests to detect and quantify phenolic compounds and to assess their antioxidant capacity by different methods. Furthermore, to investigate the electronic nature of the antioxidant activity of the main compounds present in these extracts, frontier molecular orbitals (FMOs) were obtained by the DFT/B3LYP/6-31G(d,p) level of theory. **Results**: After statistical analysis of the results, a greater number of phenolic compounds and better antioxidant activity was identified in the aqueous extracts of cumin (*C. cyminum*) in all three assays performed, when compared to the other extracts tested. The theoretical model based on the Pietro method is in agreement with the experimental results. **Conclusion**: This study has an innovative proposal with the trivial antioxidant activity combined with theoretical quantum-mechanical calculations that can serve to reduce costs and time and to predict the antioxidant activity of subsequent studies.

Keywords: Bioactive Compounds; Antioxidant Activities; Density Functional Theory; Frontier Molecular Orbitals.

Resumo

Objetivos: avaliar os compostos fenólicos e atividades antioxidantes dos extratos aquosos de *C. longa*, *P. nigrum* e *C. cyminum* bem como propor um modelo quanto-mecânico para avaliar a atividade antioxidante. **Métodos**: os extratos aquosos foram preparados por meio da utilização de raízes de *Curcuma longa* L., sementes de *Piper nigrum* L. e sementes de *Cuminum cyminum*. Os extratos foram submetidos a ensaios para detectar e quantificar compostos fenólicos e atividade antioxidante por diferentes métodos. Além disso, com objetivo de investigar a natureza eletrônica da atividade antioxidante dos principais compostos presentes nesses extratos, orbitais moleculares de fronteira (OMFs) foram obtidos pelo nível de teoria DFT/B3LYP/6-31G(d,p). **Resultados**: após as análises estatísticas dos resultados, a maior quantidade de compostos fenólicos com maior atividade antioxidante foi identificada no extrato aquoso do cominho (*C. cyminum*) em todos os ensaios realizados, quando comparados com os outros extratos testados. O modelo teórico baseado no método de Pietro está concordante com os resultados experimentais. **Conclusão**: este estudo possui uma proposta inovadora com a atividade antioxidante trivial combinada com cálculos quanto-mecânicos que podem servir para reduzir custos e tempo para predizer a atividade antioxidante de estudos futuros.

Palavras-chave: Compostos Bioativos. Atividades Antioxidante. Teoria Funcional da Densidade. Orbitais Moleculares de Fronteira.

INTRODUCTION

Oxidative stress is often associated with pathological conditions such as cancer, neurodegenerative disorders, cardiovascular disease, diabetes mellitus, acute and chronic kidney disease (CKD)[1,2]. The antioxidant plays a central role in the termination of oxidative chain reactions by removing the free radical intermediates[3]. Polyphenols are secondary metabolites from plants with antioxidant potential used in the prevention of diseases related to oxidative stress[4]. Many studies have been conducted to identify new natural antioxidants[2].

Plants and their constituents have been used in the treatment of diseases since antiquity. The use of medicinal plants is an economical and accessible way to treat the population, contributing to primary health care[5]. These constituents are

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present in fruits, vegetables, whole grains and legumes and provide nutrients that are sources of biomolecules such as phenolic compounds[6,7]. Studies involving these compounds have demonstrated several biological effects as well as anti-inflammatory[8], anti-allergic[9], anticarcinogenic[1], anti-hypertensive[10], cardioprotective[11], antimicrobial and antioxidant activities[12].

Currently, antioxidants are receiving significant economic importance due to their ability to avoid deterioration, rancidity or discoloration of foods caused by oxidation[13]. In the biological environment, antioxidants protect the damage and cell death caused by free radicals besides preventing cardiovascular, neurological and/or carcinogenic diseases[14]. The antioxidants found in the diet can be used against free radicals that can occur in the food, cosmetics, beverages and also in pharmaceutical industries[15]. Inclusion of antioxidants in the diet, as well as the consumption of fruits and vegetables, are related to the decreased risk of developing diseases associated with the accumulation of free radicals[16].

Studies reveal that numerous and heterogeneous groups of polyphenols found in plants and beverages present in the human diet exhibit many activities beneficial to health[17]. Among the activities already reported in the literature, such as anticancer, anti-inflammatory and anti-apoptotic, polyphenols also have antioxidant potentials, which are underlined by various mechanisms, making these components a viable solution against different diseases induced by oxidative stress[18].

Recently, there is an increase in the consumption of natural foods and food ingredients with potential medicinal use. Curcuma longa, *Cuminum cyminum* and *Piper nigrum* are commonly used as condiments in preparations and the use of these in food contributed to the intake of antioxidants[19,20].

Curcuma longa belongs to the family Zingiberaceae and is usually grown in tropical and subtropical regions[17]. It has been used as a medicinal plant due to its antioxidant, anti-inflammatory[18], antimutagenic, antimicrobial and anticancer properties[21–24]. In addition, *Piper nigrum* and *Cuminum cyminum* belong to families Piperaceae and Apiaceae, respectively. They are associated with various biological activities as well as anti-inflammatory[21], antibacterial[22], antiproliferative and antioxidant activities[12,23]. Studies involving the antioxidant activity of Curcuma longa, *Piper nigrum* and *Cuminum cyminum* have been performed[23].

Techniques for extracting phenolic compounds from plant materials have been reported[1,25]. Extraction in hot water is considered to be safe, low cost and environmentally friendly[26].

The aqueous extracts of Curcuma longa, *Piper nigrum* and *Cuminum cyminum* were divided into different groups and their antioxidant activity was evaluated in vitro by different methods: total antioxidant capacity (TAC), reduction power and iron chelation. For the comparison between the different concentrations within one group, the One-way ANOVA test was used associated with the Tukey multiple comparison tests, with alpha = 5.0%. For the comparison of the results between the different groups, statistical significance was determined by the Sidak-Bonferroni method, with alpha = 5.0%.

In this context, Density Functional Theory (DFT) studies can investigate the electronic nature of the antioxidant activity of the main phenolic compounds present in these aqueous extracts. The quantum-mechanical calculations of frontier molecular orbitals (FMOs) can obtain information about the nature of the electron transfer in chemical reactions, and determine reactivity indices, for instance: chemical potential, global electrophilicity index and global hardness and softness, that assistance in the description of reactivity of chemical species[27].

Quantum-mechanical calculations were performed using the DFT/B3LYP/6-31G(d,p) level of theory. The theoretical and in vitro results were compared and some models disagree, but this computational quantum-mechanical model based on the Prieto method is innovative and can be used for the total antioxidant capacity test (TAC) prediction[28]. Therefore, this analysis can serve as a parameter to make a classification of the antioxidant potential of extracts of antioxidant plants previously studied and thus guide their uses in different situations. It can also be used as a guide for the selection of samples to be used in vivo, to reduce the number of extracts and thus the number of animals needed in the tests.

METHODS

Preparation of plant extracts

In this study, we used commercial products of *Curcuma longa* L., *Piper nigrum* L. and *Cuminum cyminum* purchased at a local market. The roots of the *Curcuma longa* L. were cut into slices, seeds of the *Piper nigrum* L. were lightly ground and the seeds of *Cuminum cyminum* were used in their natural form.

Aqueous extracts of *Curcuma longa* L., *Piper nigrum* L. and *Cuminum cyminum* were prepared by heating with water (1:5, w/d) at a constant temperature of 100 ºC for 5 min. The extracts obtained were filtered through paper and analyzed for content of total phenolic compounds and antioxidant activity.

Total phenolics contents of Curcuma longa, *Cuminum cyminum* and *Piper nigrum* extracts

The measurement of phenolic compounds was performed by the reduction of the Folin Ciocalteau reagent by the phenolic compounds in the test sample, at room temperature and protected from light. This reduction promotes a change in the color from yellow to green/blue, which can be monitored by the spectrophotometer at a wavelength of 760 nm. This method has been described by Singleton and co-workers[29].

Total antioxidant activity determination

In the total antioxidant capacity test, the sample's ability to donate electrons to the molybdenum (VI), forming the molybdenum (V), was verified. The reduced molybdenum is

able to associate with the phosphate in solution, resulting in a complex called phosphomolybdate. In acidic pH, this complex acquires a greenish color that can be measured in a spectrophotometer at L= 695 nm.[28] Ascorbic acid is used as the standard for this test.

Reducing power

The reducing power of the samples was evaluated by reducing potassium ferricyanide to potassium ferrocyanide, using the method described by Athukorala and Wang.30 The extracts were mixed with phosphate buffer (0.2 M at pH 6.0), potassium ferricyanide (1%) and iron chloride, and incubated for 20 min at 50 °C. The reaction was stopped by adding 10% TCA (trichloroacetic acid) and read on the spectrophotometer at 700 nm. The test result is expressed as a percentage of the activity shown by the standard of ascorbic acid at a concentration of 0.1 mg/mL.

Iron chelating

To check the iron-chelating capacity, the extracts were added to a solution with $FeCl_2$ (2 mM) and ferrozine (5 mM), at room temperature. Fe^{2+} in solution forms a complex with ferrozine, acquiring a pink color that can be measured on the spectrophotometer at λ = 562 nm[31]. The greater the capacity of the extracts tested to chelate free iron, the less iron is available to form the complex and, consequently, the lower the intensity of the color of the solution.

Computational details

The geometries and calculations for the phenolic compounds studied were performed by the Density Functional Theory (DFT) method with hybrid generalized gradient approximation functional B3LYP and 6-31G(d,p) basis set implemented in Gaussian 16 program package.[32] For the molybdate compound, the LANL2DZ basis set was used for the molybdenum atom in its highest oxidation state (+6) and the other atoms, 6-31+G(d,p) basis set was used. Frequency calculations to analyze the vibrational modes of all studied species were carried out to verify whether the optimized geometries correspond to a minimum on the potential energy surface or transition states. In an attempt to reproduce the real medium of the researched molecules, the Polarizable Continuum Model (PCM) with the Integral Equation Formalism (IEF) was used as a solvation model[33].

Conceptual Density Functional Theory is a powerful tool for the elucidation, analysis and interpretation of the study of chemical reactions[34–37]. Based on the pioneering work of Parr and Yang, useful quantum chemical parameters have been derived from DFT. These parameters allow a qualitative and quantitative description of the chemical reaction's reactivity[34].

To obtain quantitative values of the DFT parameters, calculations of molecular density, the energy of the system, and orbital energies are required. Specifically, the frontier orbitals, HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) are calculated[38,39]. The HOMO-LUMO interpretation for reactivity started with the Fukui that studied the reactivity of aromatic compounds.[40] The related energy eigenvalues LUMO and HOMO (εLUMO and εHOMO, respectively) and their energy gap (Δε = εLUMO - εHOMO) reflect the chemical reactivity of the molecule[41,42].

According to Koopman's theorem,[43] the ionization potential (I) can be estimated as the negative HOMO energy:

$$I=-\varepsilon_{HOMO} \quad (1)$$

The electron affinity (A) can be estimated as the negative value of LUMO energy, given by:

$$A=-\varepsilon_{LUMO} \quad (2)$$

and the chemical potential, μ, which measures the scaping tendency of an electron from equilibrium, is defined as:

$$\mu=(\varepsilon_{LUMO}+\varepsilon_{HOMO})/2 \quad (3)$$

The global hardness (η)[44], can be approximated in terms of ionization potential and electron affinity by using Janak's theorem:

$$\eta=(I-A)/2 \quad (4)$$

The global softness (Θ) is defined as the inverse of /:

$$\Theta=1/\eta \quad (5)$$

In addition, the global electrophilicity index (ω),45 is given by:

$$\omega=\mu\text{^}2/2\eta \quad (6)$$

RESULTS

Total phenolics contents of *Curcuma longa*, *Cuminum cyminum* and *Piper nigrum* extracts

The phenolic compounds present in aqueous extracts of *Curcuma longa* (AECl), *Cuminum cyminum* (AECc) and *Piper nigrum* (AEPn) are depicted in Figure 1. An equivalence of 11.16 ± 2.19 mg of gallic acid (GA) per gram of extract was detected in AECl, 107.77 ± 10.51 mg of GA / g in AEPn and 440.87 ± 12.77 mg of GA / g in AECc.

Antioxidant activities of *Curcuma longa, Cuminum cyminum* and *Piper nigrum* extracts

Antioxidant activities of *Curcuma longa*, *Cuminum cyminum* and *Piper nigrum* extracts (AECl, AECc and AEPn, respectively) were measured by three different methods: total antioxidant capacity (TAC), reduction power and iron chelation. Initially, the extracts

were analyzed by the total antioxidant capacity test (TAC). In this test, the AECc stood out with an activity corresponding to 136.38 ± 18.09 mg of ascorbic acid equivalent (AA) per gram of extract. This activity is higher than that detected for AEPn, whose activity corresponds to 25.94 ± 4.15 mg of AA equivalent and higher than the activity found for AECl, 16.98 ± 1.47 of AA equivalent (Figure 2).

Figure 1. Total phenolic content of *Curcuma longa* (AECl), *Cuminum cyminum* (AECc) and *Piper nigrum* (AEPn) extracts produced by decoction in hot water. The results are expressed in mg of gallic acid equivalent (GA) per g of extract. The (*) and (#) symbols mean a significant difference between the different groups.

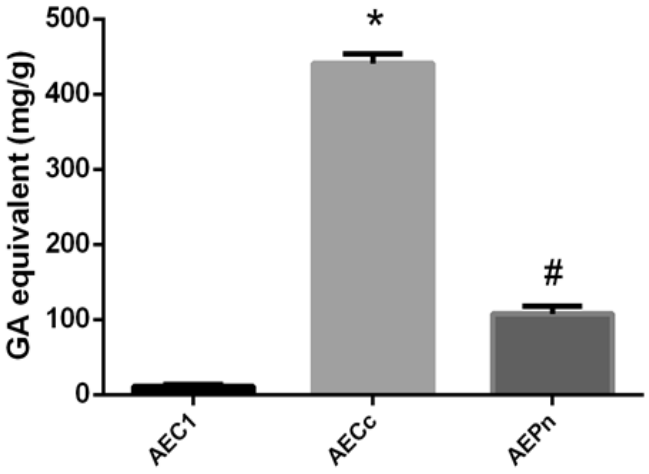
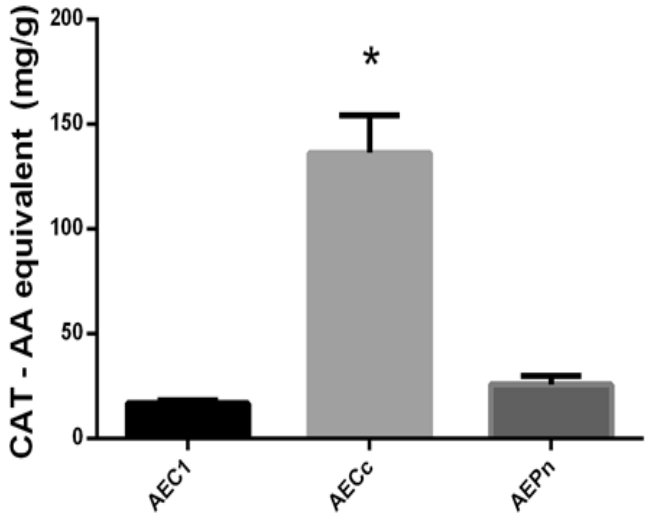


Figure 2. Total antioxidant capacity of aqueous extracts of *Curcuma longa* (AECl), *Cuminum cyminum* (AECc) and *Piper nigrum* (AEPn). The results are expressed in mg of ascorbic acid equivalent (AA) per g of extract. The (*) symbol means a significant difference between the other groups tested.



Regarding the reducing power assay, the AECl, AECc and AEPn extracts showed a dose-dependent activity (Figure 3). In addition, all extracts tested showed iron-chelating activity in dose-dependent, and the profile is more evident in the results obtained for AECl (Figure 4).

Figure 3. Reducing power of aqueous extracts of *Curcuma longa* (AECl), *Cuminum cyminum* (AECc) and *Piper nigrum* (AEPn). The results are expressed as a percentage (compared to a concentration of 0.2 mg/mL ascorbic acid). Different letters mean a significant difference between concentrations in the same group ($p < 0.05$). The (*) and (#) symbols mean a significant difference between different groups.

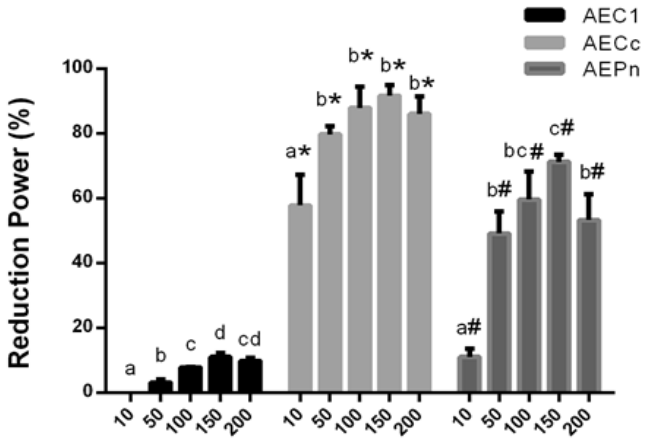
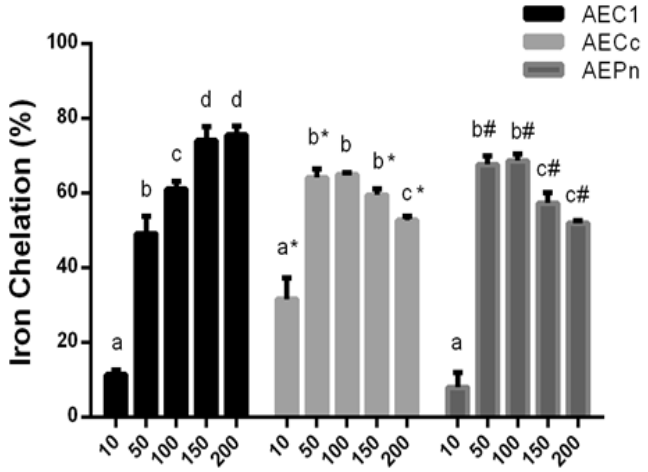


Figure 4. Iron chelating effect of aqueous extracts of *Curcuma longa* (AECl), *Cuminum cyminum* (AECc) and *Piper nigrum* (AEPn). Different letters mean a significant difference between concentrations in the same group ($p < 0.05$). The (*) and (#) symbols mean a significant difference between the concentrations of different groups.



Computational studies

Figure 5 shows the optimized geometries of the main phenolic compounds present in extracts AECl, AECc and AEPn, called curcumin, thymol and capsaicin (Figures 5A, 5B and 5C, respectively) at the B3LYP/6-31G(d,p) theoretical level. These structures were used to obtain the quantum-mechanical parameters (Table 1).

Figure 5. Optimized geometries of the molecules curcumin (a), thymol (b), and capsaicin (c) using DFT at the B3LYP/6-31G(d,p) theoretical level.

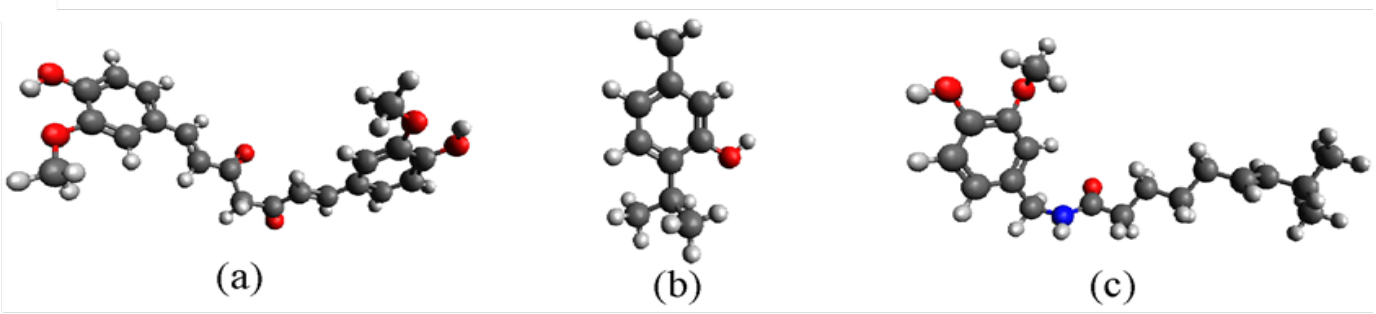


Table 1. Calculated Quantum chemical parameters. Energy value of HOMO orbital (ε_{HOMO}), energy value of LUMO orbital (ε_{LUMO}), energy gap (Δε), total dipole moment (μ), ionization potential (I), electron affinity (*A*), hardness (η), softness (σ) and global electrophilicity index (ω) for studied species obtained using DFT at the B3LYP functional and 6-31G(d,p) basis set.

Parameters	Curcumin	Thymol	Capsaicin
ε_{LUMO} *(eV)*	-1.9889	0.0253	-0.1180
ε_{HOMO} *(eV)*	-5.7275	-5.6120	-5.9510
Δε (eV)	3.7386	5.6373	5.8330
μ (debye)	10.3460	1.8460	7.3857
I (eV)	5.7275	5.6120	5.9510
A (eV)	1.9889	-0.0253	0.1180
η (eV)	1.8693	2.8187	2.9165
σ (eV^{-1})	0.5350	0.3548	0.3429
ω (a.u.)	1.9908	0.6921	0.7893

HOMO and LUMO orbitals and energy gap (in electronvolt, eV) for the molecules curcumin (a), thymol (b), and capsaicin (c) using B3LYP/6-31G(d,p) level of theory are shown in Figure 6.

The electronic transfer model based on the Pietro method is shown in Figure 7.

This model has its origin in the HOMO and LUMO frontier molecular orbitals.

Figure 6. HOMO and LUMO orbitals for the molecules curcumin (a), thymol (b), and capsaicin (c) using DFT at the theoretical level B3LYP/6-31G(d,p). The energy gap between HOMO and LUMO orbitals ($\Delta\varepsilon = \varepsilon_{LUMO} - \varepsilon_{HOMO}$) of the studied species is in electronvolt (eV).

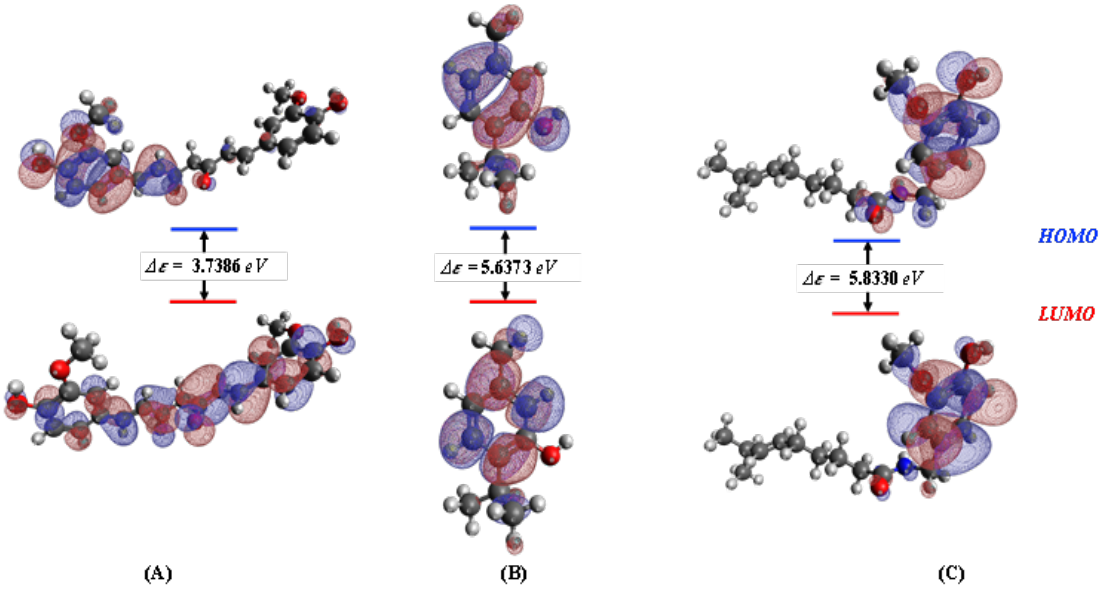
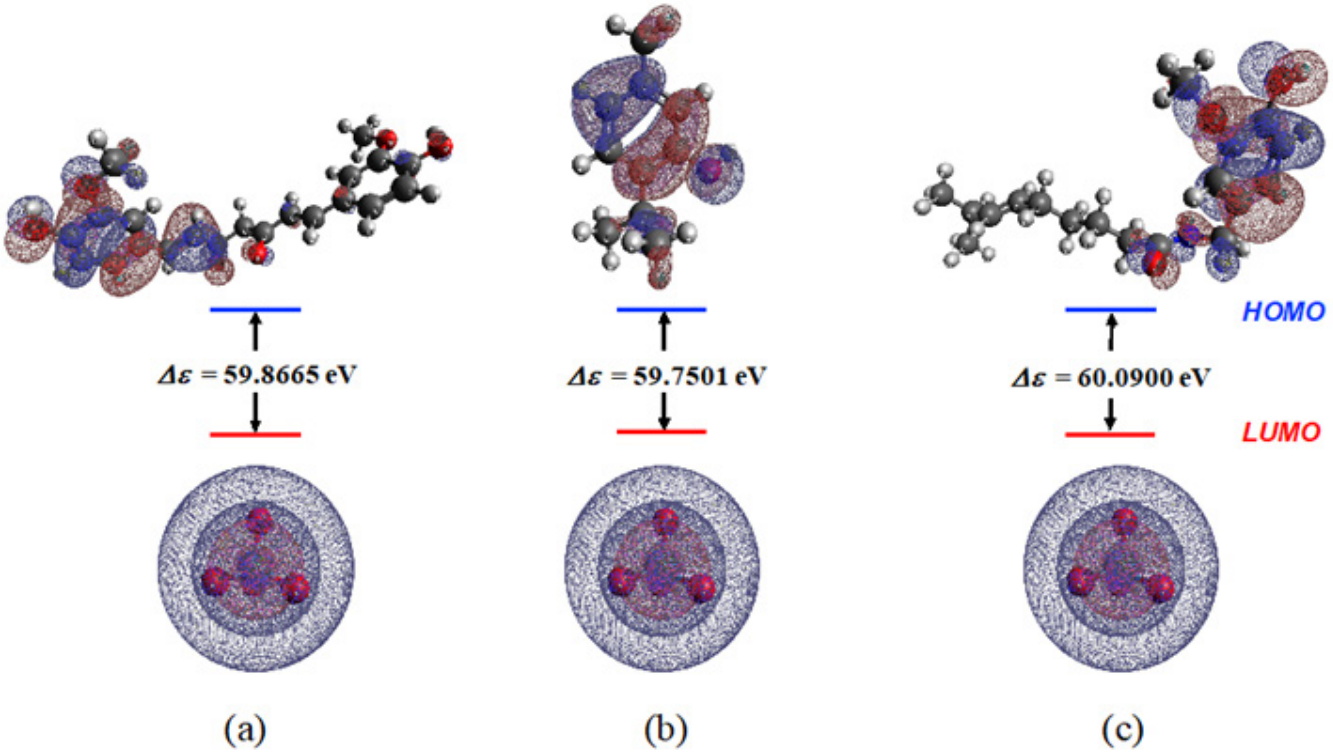


Figure 7. HOMO orbitals for the molecules curcumin (a), thymol (b), and capsaicin (c) and LUMO orbital for molybdate compound using DFT at the B3LYP/LANL2DZ for molybdenum atom and B3LYP/6-31G(d,p) for the remainder atoms. The energy gap between HOMO and LUMO orbitals ($\Delta\varepsilon = \varepsilon_{LUMO} - \varepsilon_{HOMO}$) of the studied species is in electronvolt (eV).



DISCUSSION

We can see that the number of phenolic compounds present in *C. cyminum* seeds was much higher than that of AECl and AEPn. The large quantity of phenolic compounds in *C. cyminum* has been reported by other authors.[23,46–48] In a study where the quantification of phenolic compounds was performed by HPLC - QqQ-MS / MS, it was seen that the concentration of polyphenols was higher in cumin (about 65 µg / g DW), according to the antioxidant capacity values and total polyphenols obtained.[20]

Phenolics are active compounds whose structures are quite varied. They can be divided, according to their solubility, into two main categories. The first consists of soluble phenolic compounds, such as flavonoids and quinones, often found in the vacuole of plant cells. The second category consists of insoluble compounds, such as lignin, generally detected in the cell wall[49].

Looking at Figure 1, one can observe the great variation in the concentration of phenolic compounds among the three species tested and this result can reflect the different categories of phenolics present in each one of them. Bearing in mind that the extraction carried out in this research was aqueous, it is suggested that the extract obtained from cumin (AECc) is rich in soluble phenolics, whereas the other extracts might be rich in insoluble phenolics, that would be better extracted in organic solvents.

Taking into account the fact that the number of phenolics in AECc was the highest (Figure 1) and their total antioxidant capacity was also the highest in this assay (Figure 2), it can be suggested that these compounds directly influence the capacity of the extract in electron donation quantified by TAC

Regarding the reducing power assay, all the three extracts showed a dose dependent activity, as can be seen in Figure 3, reaching a plateau in the dosages of 100 and 150 µL and a tendency to decay in the dosage of 200 µL.

Despite all of them having a similar activity profile, AECc stood out with a higher percentage of reduction, whose maximum activity was 91.60% ± 3.35 (when administered 150 µL of extract). For AEPn and AECl, lower activities corresponding to 71.23% ± 2.18 and 11.02% ± 0.95 were identified, respectively, at 150 µL dosages (Figure 3).

Substances with a reduction potential can react with potassium ferricyanide (Fe^{3+}) to form potassium ferrocyanide (Fe^{2+}), which reacts with ferric chloride to form the ferric ferrous complex. This reaction determines the reducing power.[50] The high reducing power of AECc and AEPn can be due to the hydrogen donation capacity, and phenolic compounds appear to be responsible for this antioxidant activity because both have in their composition a phenolic amount greater than AEC1 (Figure 1).

Other researchers also found in their work a link between the number of phenolic compounds and the antioxidant potential of

the samples tested. Guorong Du and co-workers[51] investigated the antioxidant potentials of eight different genotypes of Actinidia and the relationship with their total polyphenols and vitamin C content. They reported with this study that there are highly significant linear correlations between the antioxidant capacity of Actinidia fruit samples investigated and the content of polyphenols and vitamin C present in the sample[51].

In addition to this, other works also bring similar reports, such as that of Lei Jin and co-workers[52], which speculates that the phenolic compounds present in the extracts of *Lilium* bulbs largely explain their different antioxidant abilities.

In the iron chelation test, it was possible to identify the antioxidant potential of the extracts indirectly. This test measures the ability of the extract to reduce free iron. the most abundant transition metal in biological systems, it is able to catalyze oxidative changes in cellular components, such as lipids and proteins and to interact with hydrogen peroxide (H_2O_2) in a Fenton and Haber-Weiss reaction, leading to the formation of a powerful oxidizing radical (hydroxyl)[53].

In addition, transition metals, such as iron and copper, stimulate lipid peroxidation via the Fenton reaction by decomposing lipid hydroperoxides into peroxyl and alkoxy radicals that can accelerate and perpetuate the chain reaction of this lipid peroxidation[54]. To avoid this chain of cellular damage, the concentration of free iron needs to be finely regulated and chelating agents are among the most promising tools for maintaining the concentration of this metal at controlled physiological levels[55].

In Figure 4, it can be seen that all three extracts tested showed iron chelating activity, this activity is dose dependent, and the profile is more evident in the results obtained for AECl. With the other extracts tested, maximum activity was achieved quickly in the second dosage administered in the trial.

AEC1 showed an iron chelating activity of 75.52% ± 2.33 at the maximum dose (200 µL), the highest activity observed when compared to the other extracts. However, with considerably lower doses (50 µL), AECc achieved a chelating activity of 64.13% ± 2.22 and AEPn 67.63% ± 2.33.

From the results shown above, we can suggest that the aqueous extracts of *Cuminum cyminum* (AECc) have a highest antioxidant activity than AECl and AEPn regardless of the method tested, total antioxidant capacity (TAC), reduction power or iron chelation. To elucidate the electronic nature of the antioxidant activity, quantum chemical descriptors of the main phenolic compounds present in aqueous extracts were determined and related to their experimental results.

Curcumin is present in about 2% of the dry weight of *C. longa* rhizomes, and it is considered to be the principal component of this herbaceous plant which has a potent antioxidant activity.[56,57] Thymol and capsaicin are present in *C. cyminum* and P. nigrum, respectively, and both phenolic compounds are associated with antioxidant activity.25-58 In addition, the antioxidant capacity of an extract cannot be assigned only by the total phenolic compounds content, being necessary also the structural study of the compound with antioxidant activity.[59] The antioxidant activity of the phenolic compounds can be related to their geometries and electron structures by using Density Functional Theory (DFT)[60–63].

The Frontier Molecular Orbitals (FMO), the HOMO and LUMO orbitals are the main orbitals related to chemical reactivity, where their energy gap (Δε) reflects the chemical reactivity of the molecule[41,42]. According to the Δε values shown in Table 1 for curcumin, thymol, and capsaicin (3.7386 eV, 5.6353 eV and 5.8330 eV, respectively), curcumin has the lowest Δε value, followed by thymol and capsaicin. Thus, the order of increasing Δε values was curcumin < thymol < capsaicin (Figure 6). However, this result is in disagreement with experimental results for the antioxidant activity of extracts AECl, AECc and AEPn. The higher HOMO energy (ε_{HOMO}) indicates the more reactive molecule in the reaction with electrophiles[64]. The ε_{HOMO} values for the phenolic compounds studied agree with their experimental value where the decreasing order of εHOMO values was thymol > curcumin > capsaicin (Table 1). With respect to LUMO energy (ε_{LUMO}), the lower the ε_{LUMO} the more reactive the molecule is in the reaction with nucleophiles.64 The ε_{LUMO} values agree with their experimental value where the decreasing order of εLUMO were thymol > capsaicin > curcumin (Table 1). The ionization potential (I) and electron affinity (A) descriptors are calculated by the FMO energies[43]. The I, defined as the negative of εHOMO, describes the minimum energy necessary to remove one electron in the system at the ground state.[65] The I values are shown in Table 1. Capsaicin has the lowest I (5.9510 eV) followed by curcumin (5.7275 eV) and thymol (5.6120 eV). The A, defined as the negative of ε_{LUMO}, is the energy difference between the neutral and the anionic species[65]. Among the studied species, thymol has the lowest A value followed by capsaicin and curcumin.

Among all quantum-chemical above-mentioned parameters, only Δε values are not in agreement with the experimental results of antioxidant activity. Therefore, it was necessary to build another electronic model to explain this nature.

The model was built based on the Prieto method that has been developed for the quantitative determination of antioxidant activity[28]. This method is based on the reduction of Mo (VI) to Mo (V) by the sample analyte. Thus, these electrons transfer from nucleophile (analyte) to the electrophile (Mo^{6+}) can be interpreted through Frontier Molecular Orbitals (FMO) HOMO and LUMO. The HOMO orbital represents the ability to donate electrons (nucleophile) and LUMO as an electron receptor (electrophile). As already aforementioned, the HOMO-LUMO energy gap (Δε) is an important stability index[66]. A large Δε implies high stability and, therefore, low reactivity for the molecule in chemical reactions.[67] On the other hand, a low Δε value implies a high reactivity for the molecule.

We can see in Figure 7 that the electrophile considered in this model was the molybdate oxoanion with molybdenum in its highest oxidation state (VI). The calculated Δε values show that thymol has the lowest value (59.7501 eV) concerning curcumin (59.8665 eV) and capsaicin (60.0900 eV). Thus, the increasing order of reactivity is capsaicin < curcumin < thymol. This result is in agreement with the experimental for antioxidant activity (Figure 2). Therefore, we can suggest that this computational quantum-mechanical model based on the Prieto method is innovative and can be used to the total antioxidant capacity test (TAC) prediction[28].

CONCLUSIONS

In this study, we successfully built a theoretical model that suggests inferences into the electronic behavior of the antioxidant activities of the compound's capsaicin, curcumin and thymol. This model was based on the Prietro method where molybdenum (VI) is reduced to molybdenum (V) by the antioxidant species. Frontier molecular orbitals (FMO) HOMO and LUMO in nucleophilic and electrophilic species, respectively, were used. The model successfully described the electronic transfer from the antioxidant species to the molybdate being in full agreement with the experimental antioxidant activity. However, to confirm this model, greater insight into the mechanistic aspects between antioxidants and molybdenum is necessary. Therefore, this work is innovative because the theoretical antioxidant model can serve as a more rational study, yielding lower costs and less time for the investigation of experimental antioxidant activity.

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