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PAPER

Xanthones as antioxidants: A theoretical study on the thermodynamics and kinetics of the single electron transfer mechanism

Ana Martínez,*[a] Elizabeth Hernández-Marin[a] and Annia Galano[b]

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Mangosteen (*Garcinia mangostana*) is considered the queen of the tropical fruits. It has a dark red pericarp that is rich in bioactive compounds including xanthones, which have been classified as very good antioxidants from several experimental results. In this work, the antioxidant properties of twenty xanthones isolated from the pericarp of *Garcinia mangostana* are studied considering the single electron transfer mechanism (SET). According to their most acidic pK_a value, under physiological conditions the monoanionic form is present in significant amounts. For this reason, eight deprotonated xanthones are also considered in this study. Quantum chemical calculations were performed in order to assess their free radical scavenging capacity in terms of vertical ionization energies and vertical electron affinities. With these two chemical descriptors it is possible to construct a map that allows a straightforward comparison of the electron transfer viability between any pair of reactants. Such a map for the studied xanthones and the free radicals ·OH and $O_2^{\cdot-}$, in aqueous solution, indicates that xanthones can either donate or accept electrons in order to deactivate free radicals. A new relationship between the ionization potential and the electron affinity is proposed to predict the thermochemical viability of the SET processes. The electron transfer reactions between xanthones and ·OH or $O_2^{\cdot-}$ are endergonic and, therefore, thermodynamically unfeasible. However, the reaction of deprotonated xanthones with ·OH is exergonic. Thus, the deprotonated xanthones are more reactive than the neutral species through the SET mechanism. The monoanions of xanthones, which are present under physiological conditions were found to react with ·OH at diffusion-limited rates.

1. Introduction

Mangosteen (*Garcinia mangostana* Linn) is a very popular fruit considered the "queen of the tropical fruits" in South East Asia. It belongs to the Guttiferae family[1] and it is commonly cultivated in Thailand, Malaysia, and Indonesia. It has two portions: the edible soft juicy fraction that is milky white and the dark red pericarp rich in bioactive compounds as anthocyanins and xanthones. Anthocyanins have been reported as potent free radical scavengers and are believed to be contributors to the health benefits arising from consuming fruits and vegetables.[2,3] The major secondary metabolites of mangosteen are xanthone derivatives,[4–6] some of which have been reported to show antimycobacterial,[7] antifungal[8] with some cytotoxic effects,[9] and antioxidant[10–12] activities.

Over the past decade, the chemical behavior of xanthones as antioxidants has become the subject of intense experimental research and several antioxidant properties have been reported for α-mangostin, the first xanthone isolated from mangosteen fruit.[13] Within the studies on the free radical scavenging capacity of xanthones, Williams *et al.*[14] and Mahabusarakam *et al.*[15] found that they decrease the human low-density lipoprotein oxidation induced by copper or peroxyl radicals, and prevent the decrease in α-tocopherol levels induced by low-density lipoprotein oxidation. Jung and co-workers[16] performed the structure elucidation of 14 different xanthones previously isolated from the pericarp of *Garcinia mangostana*, and reported an evaluation of their antioxidant activity. More recently, α-mangostin was experimentally described as being able to deactivate some free radicals.[17]

It is important to analyze the antioxidant properties of xanthones since there are many epidemiological studies (reviewed in ref. 18) reporting a correlation between diverse pathologies and the dietary consumption of antioxidant nutrients. Antioxidants trap free radicals that cause oxidative damage and delay or inhibit the oxidative chain reactions. The most important effect of antioxidants is the reduction of the frequency of degenerative diseases such as Alzheimer's, heart disorders,

[a]*Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Circuito Exterior S. N., Ciudad Universitaria, CP 04510 México DF, México. E-mail: martina@iim.unam.mx; Fax: (+5255)5622-4596; Tel: (+5255)5622-4596*
[b]*Departamento de Química, Universidad Autónoma Metropolitana-Iztapalapa, San Rafael Atlixco 186, Col. Vicentina. Iztapalapa, CP 09340 México DF, México*

inflammation, arthritis, immune system decline, brain dysfunction, and cataracts.[19] To scavenge free radicals, one of the viable mechanisms is single electron transfer (SET).[20–23] Such a mechanism can take place by electron transfer to (I) or from the free radical (II):

$$R^{\cdot} + \text{anti} \rightarrow R^{-} + \text{anti}^{\cdot+} \quad \text{(I)}$$

$$R^{\cdot} + \text{anti} \rightarrow R^{+} + \text{anti}^{\cdot-} \quad \text{(II)}$$

In reaction I, the free radical scavenger acts as an antioxidant whilst it is an antireductant in reaction II. The relative importance of these pathways depends on diverse factors, including the structural features of the reacting antioxidant (anti) and the nature of the reacting free radical ($R^{\cdot}$).[21] The reaction is regulated by the ionization energy and the electron affinity of both the radical scavenger and the free radical. Regardless of which of them is the electron donor and which is the electron acceptor; a good electron donor (either the antioxidant or the free radical) should have low ionization energy and will give electrons to a good electron acceptor (with high electron affinity). Considering all these features, it is possible to propose relative efficiencies of the scavengers within the assumption that they work under the same mechanism.

The main goal of the present work is to analyze the electron transfer power of a large series of xanthones and to identify those that are more efficient for scavenging free radicals. Considering that under physiological conditions the monoanionic species are expected to be present in significant amounts, eight deprotonated xanthones are also considered. These molecules were selected in order to have a representative group of deprotonated xanthones. As analyzed later in this report, the electron donor acceptor capacity of these molecules is similar, and for this reason we considered unnecessary to study all the rest of deprotonated xanthones.

Quantum chemical calculations were performed in order to asses the vertical Ionization Energy (*IE*) and vertical Electron Affinity (*EA*), which were then used to predict the antioxidant capacity through SET. A discussion about the adiabatic Gibbs free energies for the SET reactions of xanthones and deprotonated xanthones with $O_2^{\cdot-}$ and $^{\cdot}OH$ is also included. These two free radicals were chosen to represent the two reaction paths: with the free radical donating an electron ($O_2^{\cdot-}$) or with the free radical ($^{\cdot}OH$) accepting an electron. Kinetic calculations have also been performed and rate constants are proposed for the monoanions, which are proposed to be the active form of xanthones through SET.

2. Theoretical methodology

Full geometry optimizations without symmetry constraints of the neutral species, anions and cations were carried out using the hybrid, three-parameter B3LYP functional[24,25] within Density Functional Theory (DFT) framework, and the 6-311G** basis set.[26–28] Re-optimization was performed for the ground states at 6-311+G* level. Harmonic frequency analyses were used to verify the optimized minima. In order to find the most stable monoanions, all the possible deprotonation sites in the selected xanthones were investigated and also optimized. The monoanions in this case are the reference. To analyze the charge transfer process of the deprotonated xanthones (monoanions), we also optimized the neutral (that is the correspondent cation) and the dianion (that in this case is the anionic system). Thermal corrections to Gibbs free energies were used to obtain the adiabatic Gibbs free energy of each specie involved in the charge transfer reaction. The stationary points were first modeled in gas phase (vacuum), and solvent effects were included *a posteriori* by single point calculations, using a polarizable continuum model, specifically the integral equation formalism (IEF-PCM)[29,30] with water as solvent for mimicking polar environments. All calculations were performed with the Gaussian 03 software.[31] The Gibbs free energies in solution were in turn computed as the PCM B3LYP/6-311+G* single point electronic energy plus the thermal corrections to Gibbs free energies from the gas phase at the same level of calculation. Some test calculations were performed with the SMD continuum model and the conclusions remained the same. Single point energy calculations at the optimized geometries were computed at B3LYP/6-311+G* level to obtain vertical *IE*s and *EA*s.

The rate constants (k) were calculated using Conventional Transition State Theory (TST)[32] and 1 M standard state as:

$$k = \frac{k_B T}{h} e^{-\left(\Delta G_{ET}^{\ddagger}\right)/RT} \quad (1)$$

where k_B and h are the Boltzmann and Planck constants, and ($\Delta G_{ET}^{\ddagger}$) is the Gibbs free energy of activation for the electron transfer reaction, which has been calculated using the Marcus theory[33] as:

$$\Delta G_{ET}^{\ddagger} = \frac{\lambda}{4}\left(1 + \frac{\Delta G_{ET}^{0}}{\lambda}\right)^2 \quad (2)$$

where ΔG_{ET}^{0} is the free energy of reaction and λ is a reorganization term. In this work a very simple approximation has been made in order to calculate λ:

$$\lambda \approx \Delta E_{ET} - \Delta G_{ET}^{0} \quad (3)$$

where ΔE_{ET} has been calculated as the non-adiabatic energy difference between reactants and vertical products. This approach is similar to that previously used by Nelsen and coworkers[34,35] for a large set of self-exchange reactions.

The calculated rate constants (k) were found to be close to the diffusion-limit. Accordingly, the apparent rate constant (k_{app}) cannot be directly obtained from TST calculations. In the present work the Collins–Kimball theory (CK) is used to that purpose:[36]

$$k_{app} = \frac{k_D k_{act}}{k_D + k_{act}} \quad (4)$$

where k_{act} is the thermal rate constant, obtained from TST calculations (eqn (1)), and k_D is the diffusion rate constant. The major assumption in the CK theory is that the reaction takes place at a specific distance (R). In this work this distance has been calculated as the sum of the radii of the reactants ($R = R_A + R_B$), and k_D has been calculated using the steady-state Smoluchowski[37] rate constant for an irreversible bimolecular diffusion-controlled reaction:

$$k_D = 4\pi R D_{AB} N_A \quad (5)$$

where R denotes the reaction distance mentioned above, N_A is the Avogadro number, and D_{AB} is the mutual diffusion coefficient of the reactants A (free radical) and B (antioxidant). In this framework, molecules are treated as non-overlapping spheres that diffuse as Brownian particles with diffusion rate k_D. The value of D_{AB} in eqn (5) has been calculated from D_A and D_B according to Truhlar's assumption,[38] which considers that the relative motion of A and B is that of B diffusing with respect to A. In turn D_A and D_B have been estimated from the Stokes–Einstein approach:[39]

$$D_A = \frac{k_B T}{6\pi\eta a_A} \quad (6)$$

$$D_B = \frac{k_B T}{6\pi\eta a_B} \quad (7)$$

where k_B is the Boltzmann constant, T is the temperature, η denotes the viscosity of the solvent, in our case water ($\eta = 8.91 \times 10^{-4}$ Pa s), and a_A and a_B are the radii of A and B.

3. Results and discussion

It has been reported before, for carotenoids, that to scavenge free radicals the antioxidant species could either donate or accept an electron.[22] This means that the electron transfer reaction is regulated by the ionization energy and the electron affinity of the antioxidant and the free radical. Low ionization energy means that the molecule will donate an electron with lower energetic cost, while high electron affinity characterizes molecules that will accept an extra electron easily. In a previous work,[23] an energetic index was reported accounting for the full electron transferability. It was defined within the chemical reactivity theory as:

$$\Delta E = \chi_d - \chi_a + \frac{1}{2}(\eta_d + \eta_a) \quad (8)$$

In this equation, d and a refer to the electron donor and acceptor, respectively. The difference of the reactants' electronegativity (χ, a measure of their ability to accept electrons) is used together with the arithmetic mean of the hardness (η, a measure of the resistance to donate electrons). This equation can be easily simplified considering the definitions of χ and η as $\chi = \frac{IE + EA}{2}$ and $\eta = IE - EA$. With these equations,

$$\Delta E = \left[\frac{IE_d + EA_d}{2}\right] - \left[\frac{IE_a + EA_a}{2}\right] + \frac{1}{2}[(IE_d - EA_d) + (IE_a - EA_a)]$$

$$\Delta E = \left[\frac{2IE_d - 2EA_a}{2}\right] = IE_d - EA_a \quad (9)$$

ΔE indicates the feasibility of the charge transfer reaction considering the electron donor and the electron acceptor capacity of the reactants. It is important to note that the external potential is constant in the chemical reactivity theory. For this reason, the ionization energy (IE) and the electron affinity (EA) must be vertical values. As was previously shown, ΔE is negative for exergonic reactions ($\Delta G < 0$), indicating that the reaction is thermodynamically feasible. To satisfy this condition, it is unambiguous that

$$IE_d < EA_a$$

This is a logical finding and means that, in order to transfer an electron without energetic cost, the energy to remove an electron from the donor must be lower than the energy to accept an electron of the acceptor. Considering this condition, the main issue is the identification of the electron donor and the electron acceptor. To this end, a map has been proposed[21,23] (Fig. 1) that is constructed from ionization energies and electron affinities. This map allows the classification of different species as electron donors or acceptors, and also permits a direct comparison between them. Molecules located in the lower left corner are good electron donors and poor electron acceptors. Those situated in the upper right corner are good electron acceptors and poor electron donors. Therefore the electrons will be transferred from species located at the lower left of the map to species located at the upper right. With this information it is possible to predict which molecule will be the electron donor and which one the electron acceptor. After this characterization, the correspondent IE and EA values indicate if the reaction will be exergonic, provided that no significant entropic effects are present, which is the case in SET mechanisms.

The xanthones studied in the present work are shown in Table 1. For eight of them, the deprotonated species have also been considered. The different possible monoanions for each of molecule were computed. The structures with the lowest energy were identified in each case and are those used in this work (Table 2). The acronyms used for these are the same as their parent structures, but followed by –H, indicating that they have lost a proton.

Fig. 2 presents the map for xanthones, deprotonated xanthones, ȮH and $O_2^{\cdot-}$, in water. Compared to ȮH, all the xanthones and deprotonated xanthones are better electron donors and worse electron acceptors than this free radical. They are located down to the left with respect to ȮH, and therefore they are predicted to act as electron donors to deactivate this free radical.

In water, xanthones, deprotonated xanthones and $O_2^{\cdot-}$ are localized more or less at the same position in the map. As a consequence, no electron transfer is expected to occur between xanthones or deprotonated xanthones and the superoxide radical anion. As can be seen in Fig. 2, deprotonated xanthones are better electron donors than the correspondent neutral molecules, whilst the electron affinity indicates that both have similar electron acceptor capabilities. According to these results,

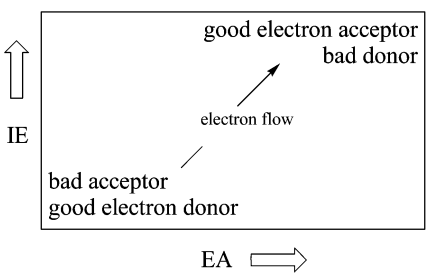


Fig. 1 Electron Affinity (*EA*) *versus* Ionization Energy (*IE*). The electron flow will be from molecules situated at the bottom left section of the map to molecules localized at the top right section of the map.

Table 1 Set of free radical scavengers (xanthones) studied in this work

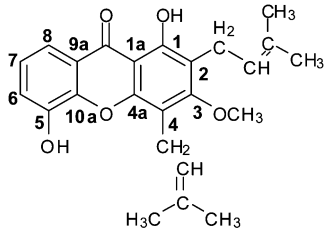
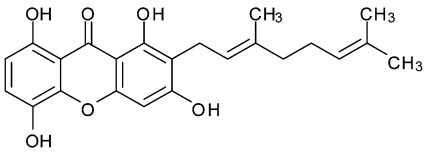
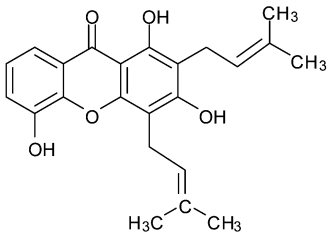
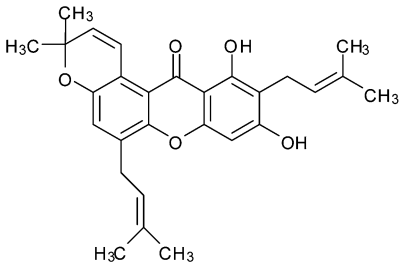
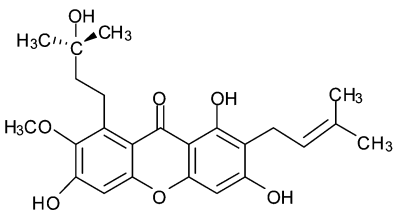
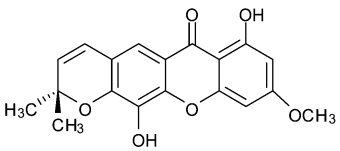
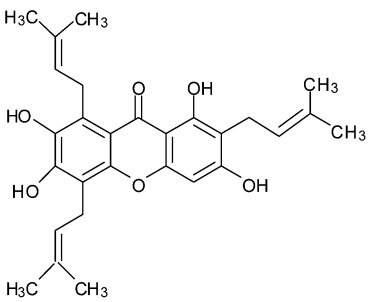
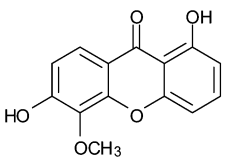
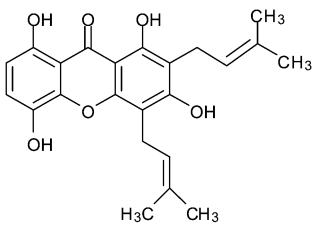
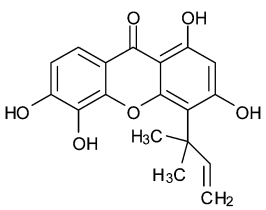
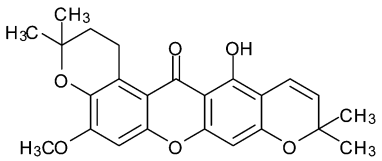
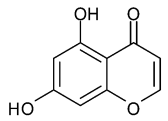
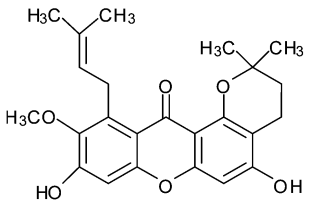
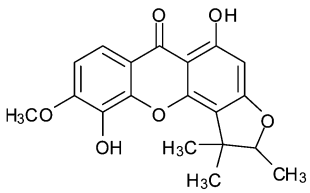
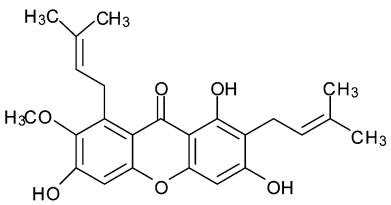
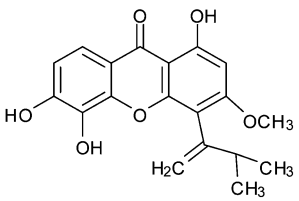
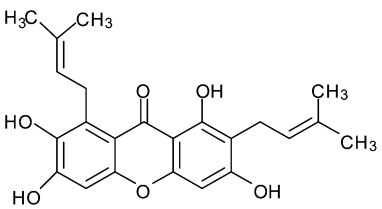
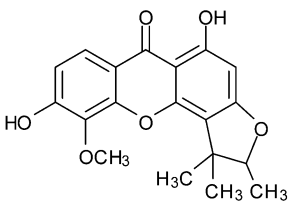
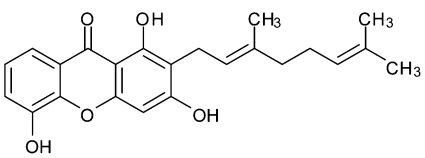
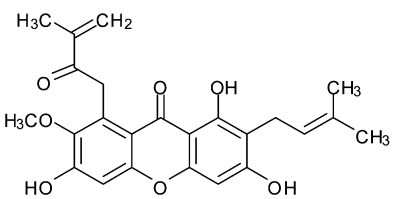
	Structure/Name		Structure/Name
1	 Cudraxanthone G	11	 smeathxanthone A
2	 8-deoxygartanin	12	 tovophylline A
3	 Garcinone D	13	 forbexanthone
4	 Garcinone E	14	 buchanaxanthone
5	 gartanin	15	 isocudraniazanthone A

Table 1 (*Contd.*)

	Structure/Name		Structure/Name
6	 garcimangosone	**16**	 5,7-dihydroxychromone
7	 1-isomangostin	**17**	 xanthone 1
8		**18**	
9	 γ-mangostin	**19**	 xanthone 3
10	 mangostinone	**20**	 xanthone 4

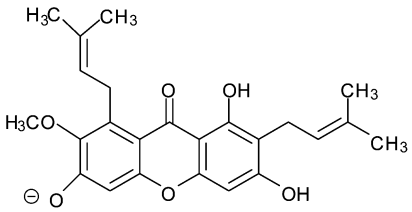
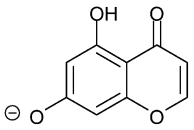
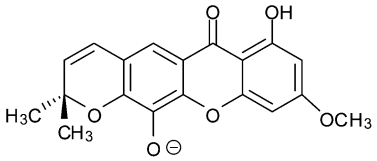
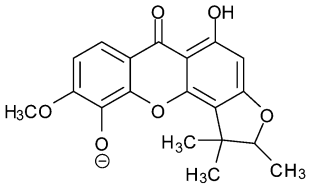
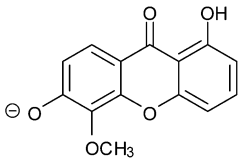
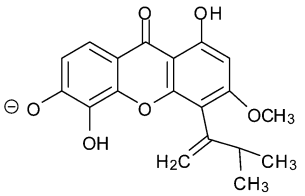
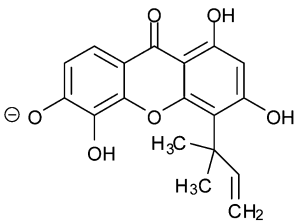
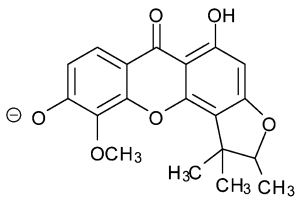
deprotonated xanthones will be better scavengers of ȮH free radical (donating an electron) than xanthones.

The localization in the map allows characterization of the electron donor and the electron acceptor capabilities, but this information does not guarantee that the reaction will be thermodynamically feasible since $IE_d < EA_a$ is a condition that is also needed. In Table 3, the *IE* and *EA* values are reported for all the molecules under study. In water, it can be expected that ȮH acts as an electron acceptor. This means that the *IE* of the donor (xanthones and deprotonated xanthones) must be smaller than the *EA* of this molecule (124.75 kcal mol^{-1}). As can be seen in Table 3, all neutral xanthones present *IE* values greater than 124.75 kcal mol^{-1}, but all the *IE* values of the deprotonated xanthones are smaller than 124.75 kcal mol^{-1}. To establish if the reaction will be exergonic, the energetic index reported before accounting for the full electron transferability (ΔE) can be used (eqn (7)). It is important to remember that this value is negative for exergonic reactions ($\Delta G < 0$).

The ΔE values for the reaction of neutral xanthones (as electron donors according to the position in the map) with ȮH are also reported in Table 3. All the ΔE values are positive, indicating that the reactions are endergonic. In contrast, the analysis of the deprotonated xanthones indicates that ΔE is negative for all the reactions with ȮH free radical, compounds **13-H** and **17-H** being the better electron donors since they show the smallest values from all the deprotonated xanthones under study.

To verify our results, we optimized the ions and calculated the ΔG values in selected cases. The Gibbs free energies of reaction for

Table 2 Set of deprotonated xanthones studied in this work

	Structure		Structure
8-H		**16-H**	
13-H		**17-H**	
14-H		**18-H**	
15-H		**19-H**	

the electron transfer processes were calculated for radicals ˙OH and $O_2^{\cdot-}$ when reacting with xanthones **8**, **13**, **14**, **16**, **17**, **18** and **19** and the deprotonated xanthones shown in Table 2. To this end, the Gibbs free energies were calculated for reaction (I) as:

$$\Delta G^0_{ET} = [G(\text{anti}^{+\cdot}) + G(R^-)] - [G(\text{anti}) + G(R^{\cdot})] \quad (10)$$

and for reaction (II) according to

$$\Delta G^0_{ET} = [G(\text{anti}^{-\cdot}) + G(R^+)] - [G(\text{anti}) + G(R^{\cdot})] \quad (11)$$

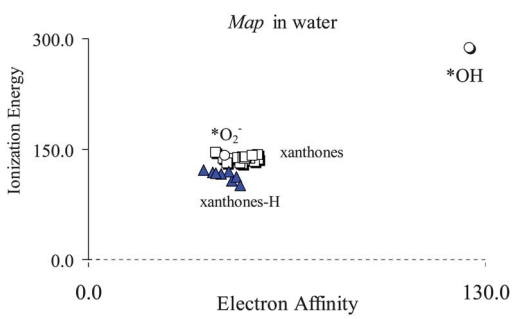


Fig. 2 Map in water that allows a straightforward comparison of the electron donor acceptor capability of xanthones (squares), $O_2^{\cdot-}$ and ˙OH (circles). Deprotonated xanthones (triangles) in water are also included.

The results are shown in Table 4. For xanthones with the free radicals considered in this study, all values are positive revealing that the reactions are endergonic. Deprotonated xanthones are predicted to have negative Gibbs free energies in water when reacting with ˙OH as an electron acceptor. These results allow us to verify the hypothesis that, in order to transfer electrons, the condition of eqn (8) must be satisfied.

In Table 5 we compared ΔE values with ΔG^0 results. It is evident that the approximation with the vertical values, which is necessary in the chemical reactivity theory to obtain ΔE, leads to the same conclusions as the thermodynamic values of the Gibbs free energies. The values are not comparable since in one case the cation and the anion are not optimized, whilst for the Gibbs free energies they were optimized. The geometry/thermal "corrections" are important but not enough to change the conclusions, *i.e.* positive ΔE values correspond with positive ΔG values, and the same for the negative results. Based on the obtained results we think that it is not necessary to perform such calculations for all the anions. Moreover the studied cases demonstrate that the vertical approach could be useful for the study of bigger systems, where the Gibbs free energies is very difficult to obtain, particularly the optimization of the anions that could be too onerous.

With these results, the main conclusion from this work is that the free radical scavenging activity of neutral xanthones is not

Table 3 Vertical Ionization Energy (*IE*) and Vertical Electron Affinity (*EA*). Energetic index (ΔE) for the full electron transferability calculated: (a) using eqn (I), considering xanthones and deprotonated xanthones as the electron donors and ˙OH as the electron acceptor; b) using eqn (II) with xanthones and deprotonated xanthones as electron acceptors and $O_2^{\cdot-}$ as the electron donor. All values in kcal mol^{-1} and calculated in water

Molecule	*IE*	*EA*	˙OH ΔE	$O_2^{\cdot-}$ ΔE
˙OH	287.67	124.75		
$O_2^{\cdot-}$	140.80	44.74		
1	135.53	55.79	10.78	85.01
2	134.95	53.49	10.20	87.31
3	139.05	50.53	14.30	90.27
4	135.02	49.73	10.27	91.08
5	130.23	50.39	5.48	90.41
6	130.82	49.70	6.07	91.10
7	137.27	44.19	12.52	96.62
8	139.26	50.67	14.51	90.13
9	136.68	46.52	11.93	94.29
10	138.02	49.05	13.28	91.75
11	130.64	45.52	5.89	95.28
12	132.64	54.58	7.89	86.22
13	136.54	53.10	11.79	87.70
14	142.16	55.57	17.41	85.24
15	137.89	50.74	13.14	90.07
16	145.22	41.71	20.47	99.09
17	138.06	51.86	13.31	88.94
18	137.07	51.20	12.32	89.60
19	139.36	51.55	14.61	89.25
20	141.14	53.67	16.40	87.13
8-H	118.50	40.75	−6.25	100.05
13-H	107.22	47.11	−17.53	93.69
14-H	119.15	45.96	−5.60	94.84
15-H	111.83	48.49	−12.92	92.31
16-H	121.09	37.71	−3.66	103.10
17-H	100.77	49.75	−23.98	91.05
18-H	116.18	43.52	−8.57	97.28
19-H	117.17	41.77	−7.58	99.03

Table 4 Adiabatic Gibbs free energy (ΔG in kcal mol^{-1}), at 298.15 K, for reactions I and II between radicals and radical scavengers from Tables 1 and 2, in water solution

Water							
$\Delta G^0_{ET} = [G(\text{anti}^{\cdot+}) + G(OH^-)] - [G(\text{anti}) + G(\dot{O}H)]$							
8	**13**	**14**	**15**	**16**	**17**	**18**	**19**
16.4	13.2	18.0	14.2	21.0	24.7	12.7	16.6
8-H	**13-H**	**14-H**	**15-H**	**16-H**	**17-H**	**18-H**	**19-H**
−8.2	−17.5	−7.6	−7.7	−0.9	−17.6	−7.9	−9.3
$\Delta G^0_{ET} = [G(\text{anti}^{\cdot-}) + G(O_2)] - [G(\text{anti}) + G(O_2^{\cdot-})]$							
8	**13**	**14**	**15**	**16**	**17**	**18**	**19**
37.2	28.8	25.9	34.6	36.8	29.6	31.6	29.9
8-H	**13-H**	**14-H**	**15-H**	**16-H**	**17-H**	**18-H**	**19-H**
41.0	34.5	39.8	36.1	38.8	36.4	37.3	39.8

governed by the electron transfer mechanism. However, deprotonated xanthones that must be present under physiological conditions can efficiently act as electron donors to deactivate free radicals.

Kinetics

In addition to the thermochemical analysis already presented, kinetic calculations were also performed to investigate the rate at which the exergonic reactions occur. The Gibbs free energies of activation and the rate constants corresponding to the electron transfers from the anions to the ˙OH free radical are reported in Table 6. As these values show, all the SET processes from monoanionic xanthones to the hydroxyl radical were found to occur at diffusion-limited rates. This confirms that, under physiological conditions, these compounds can be very efficient at deactivating one of the most damaging free radicals present in biological media.

The values of k_{SET} shown in Table 6 have been calculated as:

$$k_{SET} = f_M(A)k_{app} \quad (12)$$

where $f_M(A)$ represents the molar fraction of the anionic form (Table 7), which have been calculated using the acid constants (K_a) obtained from the pK_a values:

$$K_a = 10^{-pK_a} \quad (13)$$

Then, using the definition of the equilibrium constant, for the deprotonation equilibrium ($HA \leftrightarrow A^- + H^+$):

$$K_a = \frac{[A^-][H^+]}{[HA]} \quad (14)$$

The fraction of the anion can be easily obtained as:

$$f_M(A) = \frac{K_a}{K_a + [H^+]} \quad (15)$$

where $[H^+]$ is calculated from pH. At physiological pH (7.4), $[H^+] = 3.98 \times 10^{-8}$ M.

To calculate the pK_a values shown in Table 7 we have used the proton exchange method, also known as the isodesmic method, or the relative method, which has been proven to be reliable.[40] It involves the reaction scheme:

$$HA + Ref^- \leftrightarrow A^- + HRef$$

where HRef/Ref$^-$ is the acid/base pair of a reference compound, which should be structurally similar to the system of interest. Within this approach the pK_a is calculated as:

$$pK_a(HA) = \frac{\Delta G_s}{RT\ln(10)} + pK_a(HRef) \quad (16)$$

where the experimental value of the reference acid, HRef, is used. In our case we have chosen HRef = α-mangostin, with an estimated pK_a of 7.22.[41]

4. Conclusions

Some conclusions can be drawn from the present work, which might be relevant to the understanding of the free radical scavenging activity of xanthones:

• The maps for xanthones, deprotonated xanthones, ˙OH and $O_2^{\cdot-}$, suggest that xanthones and deprotonated xanthones can either donate or accept electrons in order to scavenge free radicals, but only the deprotonated xanthones satisfy the condition of $IE_d < EA_a$. This condition indicates that, in order to transfer an electron without energetic cost, the energy to remove an electron from the donor must be lower than the energy to accept an electron of the acceptor.

• The energetic index (ΔE) for full electron transferability and the Gibbs free energies indicate that the electron transfer reactions between xanthones and the studied free radicals are

Table 5 Energetic index (ΔE in kcal mol^{-1}) and adiabatic Gibbs free energy (ΔG in kcal mol^{-1}), at 298.15 K, for reactions I and II between radicals and radical scavengers from Tables 1 and 2, in water solution

$R^{\cdot}$ + anti → R^- + anti$^{+\cdot}$								
	8	**13**	**14**	**15**	**16**	**17**	**18**	**19**
ΔG	16.4	13.2	18.0	14.2	21.0	24.7	12.7	16.6
ΔE	14.5	11.8	17.4	13.1	20.5	13.3	12.3	14.6
$\Delta G - \Delta E$	1.9	1.4	0.6	1.1	0.5	11.4	0.4	2.0
	8-H	**13-H**	**14-H**	**15-H**	**16-H**	**17-H**	**18-H**	**19-H**
ΔG	−8.2	−17.5	−7.6	−7.7	−0.9	−17.6	−7.9	−9.3
ΔE	−6.3	−17.5	−5.6	−12.9	−3.7	−23.9	−8.6	−7.8
$\Delta G - \Delta E$	1.9	0	2.0	−5.2	−2.8	−6.0	−0.7	−1.5
$R^{\cdot}$ + anti → R^+ + anti$^{-\cdot}$								
	8	**13**	**14**	**15**	**16**	**17**	**18**	**19**
ΔG	37.2	28.8	25.9	34.6	36.8	29.6	31.6	29.9
ΔE	90.1	87.7	85.2	90.1	99.1	88.9	89.6	89.3
$\Delta G - \Delta E$	−52.9	−58.9	−59.3	−55.5	−62.3	−59.3	−58.0	−59.4
	8-H	**13-H**	**14-H**	**15-H**	**16-H**	**17-H**	**18-H**	**19-H**
ΔG	41.0	34.5	39.8	36.1	38.8	36.4	37.3	39.8
ΔE	100.1	93.7	94.8	92.3	103.1	91.1	97.3	99.0
$\Delta G - \Delta E$	−59.1	−59.2	−55.0	−56.2	−64.3	−54.7	−60.0	−59.2

Table 6 Reorganization term (λ, kcal mol^{-1}), Gibbs free energies of activation ($\Delta G^{\ddagger}_{ET}$, kcal mol^{-1}), radii of the xanthones (a_B, in Å), diffusion rate constants (k_D), and rate constants (k_{app}, M^{-1} s^{-1}), at 298.25 K

	λ	$\Delta G^{\ddagger}_{ET}$	a_B	k_D	k_{SET}
8-H	13.34	0.49	5.43	8.10×10^9	4.86×10^9
13-H	22.16	0.24	5.06	7.94×10^9	4.70×10^9
14-H	12.72	0.52	4.67	7.79×10^9	4.62×10^9
15-H	12.73	0.50	4.91	7.89×10^9	4.67×10^9
16-H	6.14	1.12	4.88	7.87×10^9	4.66×10^9
17-H	22.19	0.24	5.01	7.93×10^9	4.69×10^9
18-H	12.99	0.49	5.03	7.93×10^9	4.71×10^9
19-H	14.36	0.45	4.98	7.91×10^9	4.69×10^9

endergonic, and therefore thermodynamically unfeasible, but for deprotonated xanthones they are exergonic and thermodynamically feasible. This was confirmed by calculating the ΔG of these processes.

- The monoanions of xanthones, which are present under physiological conditions, were found to react with $^{\cdot}OH$ at diffusion-limited rates.
- Based on these results, we conclude that the electron transfer mechanism is the one involved in the antioxidant capacity of the deprotonated xanthones that are isolated from the pericarp of *Garcinia mangostana*.

Table 7 Calculated pK_a values and molar fractions of the neutral, f_M(N), and the anionic f_M (A) species

	pK_a	f_M(N)	f_M(A)
8-H	7.220	0.398	0.602
13-H	7.237	0.407	0.593
14-H	7.233	0.405	0.595
15-H	7.236	0.407	0.593
16-H	7.229	0.403	0.597
17-H	7.238	0.408	0.592
18-H	7.231	0.404	0.596
19-H	7.234	0.405	0.595

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