Electronic Supplementary Material (ESI) for RSC Advances.
This journal is © The Royal Society of Chemistry 2022

Supplementary Information (SI)

Insights into antiradical mechanism and pro-oxidant enzyme inhibitor activity of walterolactone A/B 6-O-gallate-β-D-pyranoglucoside originated from *Euonymus laxiflorus* Champ. using *in silico* study

Phan Tu Quy[1], Nguyen Anh Dzung[2], Mai Van Bay[3], Nguyen Van Bon[2], Doan Manh Dung[2], Pham Cam Nam[4], and Nguyen Minh Thong[5*]

[1] Department of Natural Sciences & Technology, Tay Nguyen University, Buon Ma Thuot 630000, Vietnam

[2] Institute of Biotechnology and Environment, Tay Nguyen University, Buon Ma Thuot 630000, Vietnam

[3] The University of Danang - University of Science and Education, Danang 550000, Vietnam

[4] The University of Danang - University of Science and Technology, Danang 550000, Vietnam

[5] The University of Danang, Campus in Kon Tum, 704 Phan Dinh Phung, Kon Tum, Vietnam

*Corresponding author: nmthong@kontum.udn.vn. (Nguyen Minh Thong)

Table of Contents

Table S1. The method to calculate rate constant following the conventional transition state theory

The rate constant (k) was calculated by using the conventional transition state theory (TST) (at 298.15 K, 1M standard state) according to the equation (1):[1-5]

$$k = \sigma\kappa\frac{k_B T}{h}e^{-(\Delta G^{\neq})/RT} \quad (1)$$

Where: σ is the reaction symmetry number ,[6, 7]

κ contains the tunneling corrections calculated using the Eckart barrier,[8]

k_B is the Boltzmann constant,

h is the Planck constant,

$\Delta G^{\neq}$ is the Gibbs free energy of activation.

The Marcus Theory was used to estimate the reaction barriers of SET reactions.[9-12] The free energy of reaction $\Delta G^{\neq}$ for the SET pathway was computed following the equations (2,3).

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

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

where ΔG_{SET} is the Gibbs energy of reaction, ΔE_{SET} is the non-adiabatic energy difference between reactants and vertical products for SET.[13, 14]

For rate constants that were close to the diffusion limit a correction was applied to yield realistic results[15]. The apparent rate constants (k_{app}) were calculated following the Collins–Kimball theory in the solvents at 298.15K;[16] the steady-state Smoluchowski rate constant (k_D) for an irreversible bimolecular diffusion−controlled reaction was calculated following the literature as corroding to equations (4,5).[15, 17]

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

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

where R_{AB} is the reaction distance, N_A is the Avogadro constant, and $D_{AB} = D_A + D_B$ (D_{AB} is the mutual diffusion coefficient of the reactants A and B),[16, 18] where D_A or D_B is estimated using the Stokes–Einstein formulation (6).[19, 20]

$$D_{A\ or\ B} = \frac{k_B T}{6\pi\eta a_{A\ or\ B}} \quad (6)$$

η is the viscosity of the solvents (i.e. $\eta(H_2O) = 8.91\times10^{-4}$ Pa s, η(pentyl ethanoate) = 8.62×10^{-4} Pa s) and a is the radius of the solute.

The kinetic study requires different considerations. Water (dielectric constants, ε = 78.35) and pentyl ethanoate (ε = 4.73) are the *de facto* standard solvents in the literature to mimic the polar and nonpolar environments in the human body.[15, 21-23] Thus, these solvents were used to model the physiological environments. The solvent cage effects were included following the corrections proposed by Okuno,[24] adjusted with the free volume theory according to the Benson correction[15, 25-27] to reduce over-penalizing entropy losses in solution. All transition states were characterized by the existence of only one single imaginary frequency. Intrinsic coordinate calculations (IRCs) were performed to ensure that each transition state is connected correctly with the pre-complex and post-complex. The kinetic calculations were performed by the *Eyringpy* code[28, 29]

Table S2. The cartesian coordinates and energies of transition states in the studied media

Name				**H3W-site 1-TS-P**	
Cartesian Coordinates				Energy (Hartree)	
O	-2.00888000	-0.67005700	-0.74427000	Zero-point correction=	0.429915 (Hartree/Particle)
O	-3.01851800	-3.48720100	1.31247100	Thermal correction to Energy=	0.461660
O	-5.50640300	-2.41293000	0.50409800	Thermal correction to Enthalpy=	0.462604
O	-5.43783100	0.38007300	-0.06691100	Thermal correction to Gibbs Free Energy=	0.366263
O	-3.08772400	1.24597000	-1.36893800	Sum of electronic and zero-point Energies=	-1790.323638
O	0.49787700	-1.82319300	0.07437200	Sum of electronic and thermal Energies=	-1790.291894
O	1.68618700	-3.49627400	-0.82368400	Sum of electronic and thermal Enthalpies=	-1790.290949
O	6.38061800	-1.60345700	-0.89441800	Sum of electronic and thermal Free Energies=	-1790.387290
O	3.84531100	1.58803700	1.48103500		
O	6.19722400	0.76587800	0.43320700		
C	-3.15636800	-2.52448100	0.28887500		
C	-4.34113700	-1.61288900	0.56198400		
C	-1.86871900	-1.69724300	0.23081000		
C	-4.37879400	-0.47616600	-0.44116200		
C	-3.03452900	0.24147600	-0.41130300		
C	-0.70138900	-2.56704600	-0.16276200		
C	1.63662800	-2.40820500	-0.30559000		
C	2.82530500	-1.55245500	-0.03636500		
C	2.71325600	-0.37008400	0.67346700		
C	4.06093600	-1.97337300	-0.55352300		
C	5.19521300	-1.19624400	-0.38271500		
C	3.85729600	0.43763600	0.84358500		
C	5.09368100	0.01432600	0.29977900		
H	-3.30696300	-3.01338700	-0.68427400		
H	-4.22736900	-1.18591000	1.56914200		
H	-1.68012200	-1.25410700	1.21925100		
H	-4.53100400	-0.87527600	-1.45187800		
H	-2.85340000	0.65337900	0.59381100		
H	-0.76728600	-2.83385100	-1.22012300		
H	-0.69244500	-3.47717700	0.43938800		
H	-3.87565100	-3.91529800	1.42321300		
H	-6.26624300	-1.84744200	0.68340700		
H	-5.54134500	1.04605100	-0.75562500		
H	1.77161700	-0.03084600	1.08886600		
H	4.13131600	-2.90672800	-1.09938400		
H	7.05746600	-0.94224400	-0.70034800		
H	3.23518900	2.33385900	0.86929700		
H	5.96032500	1.56930800	0.92341500		
C	-2.15890400	2.32911000	-1.27293400		
C	-2.33071400	3.10445800	0.01322600		

C	-0.70675700	1.95559500	-1.49364200	
C	-1.40639800	2.98801300	0.97122900	
H	-0.17415500	2.84718600	-1.83651300	
C	-0.28325400	2.03645500	0.88137100	
H	-1.48817700	3.50758400	1.91886900	
O	-0.03288000	1.46506600	-0.32032600	
O	0.37886100	1.70365700	1.82923300	
H	-0.61828600	1.16363600	-2.23526400	
H	-2.43911200	2.97438600	-2.10899900	
C	-3.56971200	3.92449000	0.15472700	
H	-3.60412100	4.43533700	1.11668100	
H	-3.62903700	4.66393500	-0.64926400	
H	-4.45084200	3.28099700	0.06727700	
O	2.61354600	1.96697400	-1.03113100	
H	1.77374700	1.50210300	-0.83562900	
O	2.68537100	2.92549300	-0.07094400	
Name				**H3W- site 2-TS-P**
Cartesian Coordinates				Energy (Hartree)
O	2.24877900	-0.56186400	0.77348300	Zero-point correction= 0.430680 (Hartree/Particle)
O	3.39520900	-3.44536600	-1.11563200	Thermal correction to Energy= 0.462046
O	5.81738600	-2.09667500	-0.57387000	Thermal correction to Enthalpy= 0.462990
O	5.53822200	0.71081400	-0.17657000	Thermal correction to Gibbs Free Energy= 0.367269
O	3.22504800	1.43886400	1.27240600	Sum of electronic and zero-point Energies= -1790.328303
O	-0.16717800	-1.92218500	0.15721800	Sum of electronic and thermal Energies= -1790.296937
O	-1.30533200	-3.71159000	0.88315000	Sum of electronic and thermal Enthalpies= -1790.295993
O	-6.10888300	-2.12832800	0.17082700	Sum of electronic and thermal Free Energies= -1790.391714
O	-3.40102300	1.53188000	-1.13176600	
O	-5.86888100	0.31989300	-0.86771000	
C	3.50668200	-2.39165100	-0.18310400	
C	4.58324000	-1.40708800	-0.60581600	
C	2.15966700	-1.67034100	-0.11540800	
C	4.58034200	-0.20357200	0.31557300	
C	3.18269700	0.40691400	0.34331000	
C	1.07488900	-2.58932700	0.39003300	
C	-1.28687600	-2.59548500	0.43046900	
C	-2.50015600	-1.79000400	0.09955900	
C	-2.34835400	-0.49559800	-0.39350000	
C	-3.75663100	-2.36322800	0.30537900	
C	-4.87973100	-1.61812800	0.00210800	
C	-3.47045800	0.25521800	-0.69803600	
C	-4.76555600	-0.29865200	-0.52271400	
H	3.75601200	-2.78053800	0.81440400	
H	4.36575200	-1.06989200	-1.62993500	
H	1.89285600	-1.32274200	-1.12376300	
H	4.82777900	-0.52153400	1.33614000	
H	2.90321300	0.77542500	-0.65736600	
H	1.19796700	-2.78265600	1.45874300	
H	1.09573300	-3.53383700	-0.15552600	
H	4.28013100	-3.80317500	-1.25408200	

H	6.51069700	-1.48151900	-0.83912500
H	5.67260000	1.39229100	0.49140100
H	-1.36348300	-0.07037600	-0.51853200
H	-3.85133400	-3.36925900	0.69363500
H	-6.75097900	-1.45637100	-0.10559200
H	-2.46169300	1.78535500	-1.28547800
H	-5.98207600	1.32215300	-0.34643600
C	2.23010900	2.45903200	1.21272300
C	2.29746900	3.23981100	-0.07996100
C	0.81300900	2.01323600	1.54006000
C	1.24485700	3.25494100	-0.90498000
H	0.29821500	2.83492500	2.04290100
C	0.06507200	2.40710700	-0.68998100
H	1.23954700	3.82912400	-1.82385900
O	0.00957200	1.65058500	0.40299000
O	-0.83202400	2.32445000	-1.50992000
H	0.82287100	1.13773600	2.18441800
H	2.52635900	3.13446500	2.01944000
C	3.57599600	3.95130100	-0.37460000
H	3.49193300	4.56530300	-1.27085700
H	3.86999600	4.57863300	0.47140100
H	4.37477700	3.21882600	-0.52922000
O	-4.84258600	2.12962700	1.14437100
H	-4.15246400	2.28468600	0.46929800
O	-6.00855900	2.25315500	0.46243600

Name			**H3W- site 3-TS-P**
Cartesian Coordinates			Energy (Hartree)
O	2.21615500	-0.64140900	0.75556000
O	3.38993500	-3.47956400	-1.18165500
O	5.81210100	-2.24484200	-0.41125400
O	5.60433200	0.54851000	0.09198500
O	3.21723400	1.29386600	1.42553800
O	-0.19440600	-1.84359000	-0.09824700
O	-1.48294700	-3.46124700	0.76728600
O	-6.10701300	-1.37791400	0.04138200
O	-3.11035600	1.78613200	-1.70994400
O	-5.59876600	1.05413300	-1.10380400
C	3.46987000	-2.47173800	-0.19650700
C	4.60728100	-1.50984800	-0.49639500
C	2.14959400	-1.70079900	-0.19193700
C	4.58236200	-0.34774000	0.47706700
C	3.20826900	0.31344800	0.44101800
C	0.99005700	-2.58715100	0.19240200
C	-1.36842300	-2.38705000	0.23442300
C	-2.49817000	-1.48729700	-0.13573000
C	-2.22894500	-0.26888400	-0.78681500
C	-3.78785600	-1.85780700	0.17767300
C	-4.86658300	-1.01599200	-0.17481300
C	-3.26269000	0.58485200	-1.10722300

Zero-point correction= 0.429928 (Hartree/Particle)
Thermal correction to Energy= 0.461663
Thermal correction to Enthalpy= 0.462607
Thermal correction to Gibbs Free Energy= 0.365363
Sum of electronic and zero-point Energies= -1790.323010
Sum of electronic and thermal Energies= -1790.291275
Sum of electronic and thermal Enthalpies= -1790.290331
Sum of electronic and thermal Free Energies= -1790.387575

C	-4.58204800	0.22068800	-0.81082800
H	3.63211200	-2.91216400	0.79747200
H	4.47447200	-1.11941800	-1.51611300
H	1.97328700	-1.29395000	-1.19825500
H	4.74765000	-0.71918700	1.49616400
H	3.01140200	0.74331100	-0.55495700
H	1.02694600	-2.82985800	1.25703000
H	1.00251000	-3.50813600	-0.39300200
H	4.26825900	-3.86838900	-1.26884100
H	6.54276300	-1.64403000	-0.59720800
H	5.72118700	1.19224000	0.79934800
H	-1.21059500	0.01204500	-1.01367300
H	-3.99949200	-2.79555400	0.67635000
H	-6.62569100	-0.64739200	0.73318000
H	-2.16045900	2.02105400	-1.75941300
H	-5.24192200	1.81020600	-1.59561000
C	2.24927200	2.33970700	1.35689200
C	2.47413700	3.23399000	0.15839100
C	0.79720000	1.90482900	1.47350000
C	1.53294400	3.32779800	-0.78730100
H	0.23568000	2.70590900	1.95972500
C	0.33635300	2.47411700	-0.79431800
H	1.64007600	3.97941000	-1.64642800
O	0.14550700	1.63366500	0.22028400
O	-0.44763200	2.46401200	-1.72549800
H	0.70932500	0.99057100	2.05481700
H	2.46114500	2.92803400	2.25333700
C	3.77390300	3.96488800	0.09306300
H	3.80321900	4.64928300	-0.75440400
H	3.94690600	4.52220900	1.01792900
H	4.59353700	3.24698000	-0.01098400
O	-6.91934500	0.16813700	1.61690900
O	-5.79748400	0.92726200	1.75283100
H	-5.83000400	1.53955300	0.99718300

Name			**H2W(-)-site 1-TS-W**
Cartesian Coordinates			Energy (Hartree)
O	-1.96762800	-0.70465000	-0.68498500
O	-3.40132700	-3.31087900	1.40042700
O	-5.71169100	-1.97995600	0.40701900
O	-5.26221400	0.78976200	-0.19580800
O	-2.77292900	1.27167000	-1.48419900
O	0.33129500	-2.00738500	0.24143400
O	1.41858700	-3.61115200	-0.88490600
O	6.03606300	-1.43986400	-1.38711300
O	3.75536000	1.12314300	1.93782100
O	5.98258300	0.60561100	0.35356900
C	-3.37721800	-2.37342300	0.33843500
C	-4.46027300	-1.32174900	0.52225700
C	-2.00455000	-1.70187600	0.33303000

Zero-point correction= 0.416790 (Hartree/Particle)
Thermal correction to Energy= 0.448808
Thermal correction to Enthalpy= 0.449753
Thermal correction to Gibbs Free Energy= 0.352519
Sum of electronic and zero-point Energies= -1789.907968
Sum of electronic and thermal Energies= -1789.875950
Sum of electronic and thermal Enthalpies= -1789.875006
Sum of electronic and thermal Free Energies= -1789.972240

C	-4.31309300	-0.21308700	-0.50654900
C	-2.89415000	0.34124100	-0.45220900
C	-0.90843900	-2.69105200	0.02296900
C	1.43918300	-2.56215700	-0.26715700
C	2.64118000	-1.75132700	-0.02331300
C	2.62895900	-0.70759700	0.89076200
C	3.80210900	-2.02237600	-0.78887100
C	4.90449200	-1.22838500	-0.64647400
C	3.75660700	0.09697500	1.04907800
C	4.94537100	-0.12086400	0.27505600
H	-3.53176300	-2.87988000	-0.62337900
H	-4.35710800	-0.88717500	1.52542300
H	-1.82422200	-1.23742300	1.31222200
H	-4.48509700	-0.61647100	-1.51169800
H	-2.69862400	0.79505900	0.52953400
H	-0.97770500	-3.01172200	-1.01804600
H	-0.96561300	-3.55849200	0.68145600
H	-4.28722700	-3.69229500	1.43611100
H	-6.40520700	-1.36430900	0.67233700
H	-5.27098900	1.43314700	-0.91527900
H	1.74804500	-0.48557400	1.47947800
H	3.80819200	-2.83788700	-1.50285500
H	6.66072500	-0.74231600	-1.12781400
H	3.63336200	1.98564600	1.41511200
C	-1.77540000	2.29446300	-1.37565000
C	-1.99683500	3.16281800	-0.16015000
C	-0.33960000	1.81890800	-1.46196600
C	-1.12515800	3.11074400	0.85282200
H	0.27131700	2.64296100	-1.83653100
C	-0.02679800	2.13680200	0.90062600
H	-1.24231100	3.71472100	1.74477500
O	0.23247600	1.40449100	-0.20058600
O	0.62283100	1.91829100	1.90071100
H	-0.24471300	0.96054600	-2.12325100
H	-1.94575900	2.90273400	-2.26665400
C	-3.21845100	4.01681900	-0.15237600
H	-3.29782900	4.59101300	0.76992800
H	-3.20255800	4.69768900	-1.00821000
H	-4.10675200	3.38617100	-0.25960400
O	3.05935800	1.92710200	-0.72565300
H	2.16192600	1.56451000	-0.57142000
O	3.23877200	2.88007600	0.20932400

Name			**H2W(-)-site 3-TS-W**
Cartesian Coordinates			Energy (Hartree)
O	1.96983000	-0.72854600	0.72529100
O	3.26834100	-3.51876800	-1.18666200
O	5.58878800	-2.50947700	0.08160700
O	5.47054800	0.28662500	0.65770700
O	2.89677800	1.16798800	1.55679200

Zero-point correction= 0.417370 (Hartree/Particle)
Thermal correction to Energy= 0.449845
Thermal correction to Enthalpy= 0.450790
Thermal correction to Gibbs Free Energy= 0.350642
Sum of electronic and zero-point Energies= -1789.871796

O	-0.38708400	-1.71029100	-0.32279300
O	-1.74810800	-3.40801500	0.20299900
O	-3.24941700	2.24894900	-1.15876700
O	-5.75635600	1.38962100	-0.84265400
C	3.23869800	-2.57880200	-0.13271100
C	4.46834700	-1.68361300	-0.16916100
C	1.97446000	-1.73059500	-0.27870200
C	4.35326100	-0.55603700	0.84436800
C	3.04346000	0.17884400	0.59341100
C	0.73103500	-2.56529700	-0.08995600
C	-1.60240400	-2.24618200	-0.11507500
C	-2.69080900	-1.27142100	-0.30480700
C	-2.41446700	0.07134900	-0.66206100
C	-3.99897700	-1.69571200	-0.09020900
C	-5.05680400	-0.80775000	-0.25286000
C	-3.45202900	0.95039800	-0.81317100
C	-4.83128400	0.55603000	-0.65334200
H	3.21048400	-3.09021900	0.83967400
H	4.54651800	-1.24041000	-1.17245700
H	1.95862900	-1.26310100	-1.27389900
H	4.33172500	-0.96808500	1.86066300
H	3.05126400	0.60520700	-0.42115400
H	0.69007400	-2.95533000	0.93020500
H	0.72345500	-3.39898700	-0.79371500
H	4.11909600	-3.97105300	-1.14883200
H	6.38333500	-1.96859800	0.01400300
H	5.50275500	0.91672700	1.38492700
H	-1.39489800	0.40130300	-0.81725800
H	-4.20095900	-2.71705600	0.20970300
H	-4.13785200	2.64008900	-1.20737200
C	2.01416900	2.25203100	1.24011000
C	2.69498300	3.22147300	0.29892100
C	0.65028300	1.85586100	0.70233200
C	2.31526900	3.26327200	-0.98229600
H	-0.03078600	2.69813100	0.84506500
C	1.32010400	2.33072700	-1.54648400
H	2.77952000	3.92906600	-1.69995600
O	0.66245400	1.52405700	-0.69562400
O	1.12426000	2.21528300	-2.73287800
H	0.26098100	0.97446100	1.20545500
H	1.85040600	2.74463200	2.20070100
C	3.78691100	4.06524700	0.86950900
H	4.28849900	4.65046600	0.10025400
H	3.37481200	4.74175200	1.62384900
H	4.51991000	3.43191400	1.37583000
O	-6.32955500	-1.19783800	-0.04550500
H	-6.76410600	-0.49679600	0.52052800
O	-6.74914000	0.40718800	1.92009200
O	-5.40892100	0.46902100	2.11989300
H	-5.14745200	-0.40944300	2.44090900

Sum of electronic and thermal Energies=	-1789.839320
Sum of electronic and thermal Enthalpies=	-1789.838376
Sum of electronic and thermal Free Energies=	-1789.938523

Name				H3W- site 1-TS-W	
Cartesian Coordinates				Energy (Hartree)	
O	-2.00068900	-0.69722500	-0.73492400	Zero-point correction=	0.429281 (Hartree/Particle)
O	-3.12339100	-3.49326500	1.29364500	Thermal correction to Energy=	0.461127
O	-5.57702600	-2.32910100	0.44267500	Thermal correction to Enthalpy=	0.462071
O	-5.38131800	0.49828900	-0.04552300	Thermal correction to Gibbs Free Energy=	0.365857
O	-3.00433200	1.24211900	-1.39945400	Sum of electronic and zero-point Energies=	-1790.345686
O	0.44487600	-1.86313500	0.05991400	Sum of electronic and thermal Energies=	-1790.313839
O	1.63951300	-3.58804000	-0.72005500	Sum of electronic and thermal Enthalpies=	-1790.312895
O	6.31657200	-1.63858300	-0.93985400	Sum of electronic and thermal Free Energies=	-1790.409109
O	3.78090000	1.51846400	1.53591300		
O	6.13947300	0.73738400	0.40755200		
C	-3.22330600	-2.51644300	0.27265400		
C	-4.38293000	-1.56998600	0.54357100		
C	-1.91154900	-1.73086100	0.24179900		
C	-4.37007200	-0.41054100	-0.43802200		
C	-2.99973900	0.25582600	-0.41349700		
C	-0.75766400	-2.62237000	-0.13968500		
C	1.58774000	-2.46725200	-0.26098100		
C	2.77463100	-1.61086500	-0.01248800		
C	2.66874900	-0.43638400	0.70728600		
C	4.00665400	-2.01834100	-0.55185400		
C	5.13433900	-1.23350600	-0.39607300		
C	3.80881800	0.37570700	0.87096200		
C	5.04147600	-0.02483900	0.29830500		
H	-3.37522900	-2.99571000	-0.70341600		
H	-4.27686600	-1.17144200	1.56113400		
H	-1.72953300	-1.28990800	1.23168200		
H	-4.55145000	-0.78366400	-1.45321800		
H	-2.79867200	0.67715400	0.58139600		
H	-0.83242900	-2.91669300	-1.18866700		
H	-0.73207400	-3.50992900	0.49271600		
H	-3.97146700	-3.95087300	1.34812200		
H	-6.30724300	-1.79881000	0.78264000		
H	-5.45313300	1.18253200	-0.72265800		
H	1.73309800	-0.10336900	1.13791000		
H	4.08160300	-2.94487900	-1.10863500		
H	7.00997300	-0.99430900	-0.73998800		
H	3.31165900	2.30128700	0.86957100		
H	5.92041800	1.54132300	0.90669600		
C	-2.08813500	2.33704500	-1.28272800		
C	-2.29566100	3.11162500	-0.00262500		
C	-0.62947000	1.98477500	-1.47816700		
C	-1.36137900	3.06255900	0.95360400		
H	-0.10040600	2.88066700	-1.81024000		
C	-0.20118900	2.16454300	0.87818200		
H	-1.46492500	3.60202500	1.88758400		
O	0.03143300	1.51656200	-0.28111300		
O	0.51786900	1.92708400	1.82472300		

H	-0.50613900	1.19037900	-2.21100000
H	-2.36028100	2.98194900	-2.12112600
C	-3.57165500	3.87047200	0.12759100
H	-3.64150800	4.37342900	1.09133100
H	-3.64987000	4.60683600	-0.67743700
H	-4.41710500	3.18362200	0.01794100
O	2.72633100	1.91851700	-1.04297400
H	1.84341700	1.52819900	-0.86837300
O	2.85106800	2.91133000	-0.12689600

Name			**H3W- site 2-TS-W**
Cartesian Coordinates			Energy (Hartree)
O	2.00344900	-0.65509000	0.69047300
O	3.85138200	-3.16246700	-1.17763600
O	5.92411400	-1.48333800	-0.19046600
O	5.09808600	1.22953300	0.24091800
O	2.52253200	1.42859300	1.44896500
O	-0.05947400	-2.19844800	-0.26227100
O	-1.14286100	-3.86639000	0.77265000
O	-5.72459300	-1.59927300	1.26012300
O	-3.35920500	1.00870700	-1.91011000
O	-5.58257000	0.52183300	-0.43846000
C	3.66007300	-2.17586900	-0.17924300
C	4.60471000	-1.00247500	-0.38829000
C	2.21943700	-1.68175600	-0.27400800
C	4.27251900	0.12864400	0.57102100
C	2.79672200	0.49472500	0.44905700
C	1.22189600	-2.77615300	0.01800800
C	-1.15038200	-2.80528500	0.18955400
C	-2.36582600	-1.98209300	-0.07251200
C	-2.28855500	-0.92973400	-0.97918300
C	-3.52111600	-2.24772600	0.66965500
C	-4.60366900	-1.40160900	0.53287600
C	-3.37244600	-0.07845000	-1.11864700
C	-4.54889400	-0.29677700	-0.35683200
H	3.83071500	-2.60063400	0.81845300
H	4.48804900	-0.63979200	-1.41816100
H	2.04089800	-1.28377600	-1.28247400
H	4.45502400	-0.20072500	1.60097800
H	2.57663600	0.89245700	-0.55192600
H	1.27033800	-3.07359500	1.06736400
H	1.38180200	-3.64168300	-0.62531300
H	4.78025000	-3.42450500	-1.15776200
H	6.54344900	-0.79524700	-0.46077500
H	5.02642500	1.88376200	0.94645500
H	-1.38678700	-0.73919400	-1.54334200
H	-3.55741100	-3.07146300	1.37134900
H	-6.35744300	-0.89343000	1.05422200
H	-2.43179500	1.22579600	-2.14823300
H	-5.27565900	1.49982200	-0.03912300

Zero-point correction= 0.429627 (Hartree/Particle)
Thermal correction to Energy= 0.461336
Thermal correction to Enthalpy= 0.462280
Thermal correction to Gibbs Free Energy= 0.366573
Sum of electronic and zero-point Energies= -1790.347737
Sum of electronic and thermal Energies= -1790.316027
Sum of electronic and thermal Enthalpies= -1790.315083
Sum of electronic and thermal Free Energies= -1790.410790

C	1.42166800	2.32819800	1.27661000
C	1.63622800	3.25483700	0.10188000
C	0.04721500	1.69019300	1.23270200
C	0.84121900	3.15786500	-0.97038800
H	-0.68120500	2.42241400	1.58636400
C	-0.15905800	2.09453700	-1.10927900
H	0.94850200	3.81014600	-1.82871800
O	-0.37432400	1.27359300	-0.08230100
O	-0.76556900	1.89642400	-2.15174400
H	0.00122700	0.79797800	1.85286900
H	1.44824100	2.92847000	2.18864100
C	2.75046100	4.23842600	0.21203700
H	2.84791800	4.83446100	-0.69444600
H	2.57515900	4.89826500	1.06689100
H	3.69105700	3.71294900	0.40104000
O	-3.51108700	1.83384600	1.02056800
H	-2.84327900	2.01629400	0.33164500
O	-4.64804400	2.44550600	0.60852600

Name	**H3W- site 3-TS-W**
Cartesian Coordinates	Energy (Hartree)

O	2.15462600	-0.67130800	0.77361600
O	3.32971700	-3.51079100	-1.16394400
O	5.76371600	-2.28777400	-0.33525800
O	5.53487100	0.53817700	0.10186200
O	3.14644300	1.26264300	1.46151900
O	-0.24773900	-1.81472200	-0.07082700
O	-1.57196100	-3.50344300	0.57054600
O	-6.15698300	-1.24626700	0.02168700
O	-3.07637800	1.86572000	-1.71616200
O	-5.61678900	1.14153200	-1.09650300
C	3.41026100	-2.50306900	-0.17174000
C	4.55912100	-1.54929500	-0.46032200
C	2.09564800	-1.72542600	-0.18340700
C	4.52515700	-0.37086500	0.49738100
C	3.15047500	0.28916200	0.46205300
C	0.92369800	-2.60179100	0.18193300
C	-1.43380000	-2.37962400	0.13891800
C	-2.54779300	-1.46037100	-0.21192000
C	-2.26034800	-0.23368700	-0.84237800
C	-3.84241500	-1.81295200	0.10252300
C	-4.89495800	-0.93436800	-0.22161700
C	-3.27147000	0.65320700	-1.13582600
C	-4.59978700	0.31195700	-0.83574900
H	3.55601400	-2.95065000	0.81998000
H	4.45296800	-1.17602500	-1.48749800
H	1.93679900	-1.30559000	-1.18636500
H	4.70070600	-0.72714400	1.51962400
H	2.94778000	0.72297100	-0.52776200
H	0.95915000	-2.87984100	1.23755000

Zero-point correction= 0.429329 (Hartree/Particle)
Thermal correction to Energy= 0.461267
Thermal correction to Enthalpy= 0.462211
Thermal correction to Gibbs Free Energy= 0.364674
Sum of electronic and zero-point Energies= -1790.343708
Sum of electronic and thermal Energies= -1790.311770
Sum of electronic and thermal Enthalpies= -1790.310826
Sum of electronic and thermal Free Energies= -1790.408363

H	0.90028000	-3.49735900	-0.43925200
H	4.18463500	-3.95720200	-1.20117500
H	6.48974000	-1.74754400	-0.66877100
H	5.63585300	1.19889400	0.79798200
H	-1.24258100	0.02859600	-1.09502700
H	-4.07512700	-2.75164800	0.58997100
H	-6.54000900	-0.58219200	0.82471700
H	-2.11550700	2.05296800	-1.77125800
H	-5.27620900	1.96360400	-1.48320800
C	2.23187300	2.35832000	1.35435400
C	2.51276000	3.20762600	0.13644100
C	0.76333700	1.99561500	1.45404800
C	1.60446400	3.27828700	-0.84368200
H	0.22429000	2.85409400	1.85847300
C	0.39778200	2.44577200	-0.85534400
H	1.75247800	3.89278400	-1.72357900
O	0.14380700	1.66365500	0.19447000
O	-0.35397400	2.39774000	-1.81708000
H	0.61090100	1.13142300	2.09563400
H	2.45754900	2.95634700	2.24012100
C	3.81879900	3.92439700	0.09586200
H	3.91920600	4.51663800	-0.81292100
H	3.91444000	4.57438500	0.97022900
H	4.63742100	3.19978300	0.14229400
O	-6.63662000	0.21548200	1.82253100
O	-5.35959300	0.65270300	1.98220900
H	-5.31274000	1.49853600	1.50175600

Table S3. Molecular docking parameters for each protein target

Protein/PDB ID	**Ligand**	**Coordinates of the Grid Box Center**	**Grid Box Size**
Cytochrome P450/ 1OG5	S-Warfarin	center_x = -20.257 center_y = 86.991 center_z = 38.581	size_x = 20 size_y = 18 size_z = 22
Lipoxygenase/ 1N8Q	Protocatecuic acid	center_x = 21.864 center_y = 2.184 center_z = 18.909	size_x = 22 size_y = 16 size_z = 10
Myeloperoxidase/ 1DNU	N-Acetyl-D-glucosamine	center_x = 39.817 center_y = -38.635 center_z = -5.308	size_x = 9 size_y = 12 size_z = 7
NADPH oxidase/ 2CDU	Adenosine-5'-diphosphate	center_x = 1.687 center_y = 9.885 center_z = 54.962	size_x = 15 size_y = 7 size_z = 16

Xanthine oxidase/ 3NRZ	Hypoxanthine	center_x = 89.018 center_y = 9.4501 center_z = 18.290	size_x = 7 size_y = 10 size_z = 9

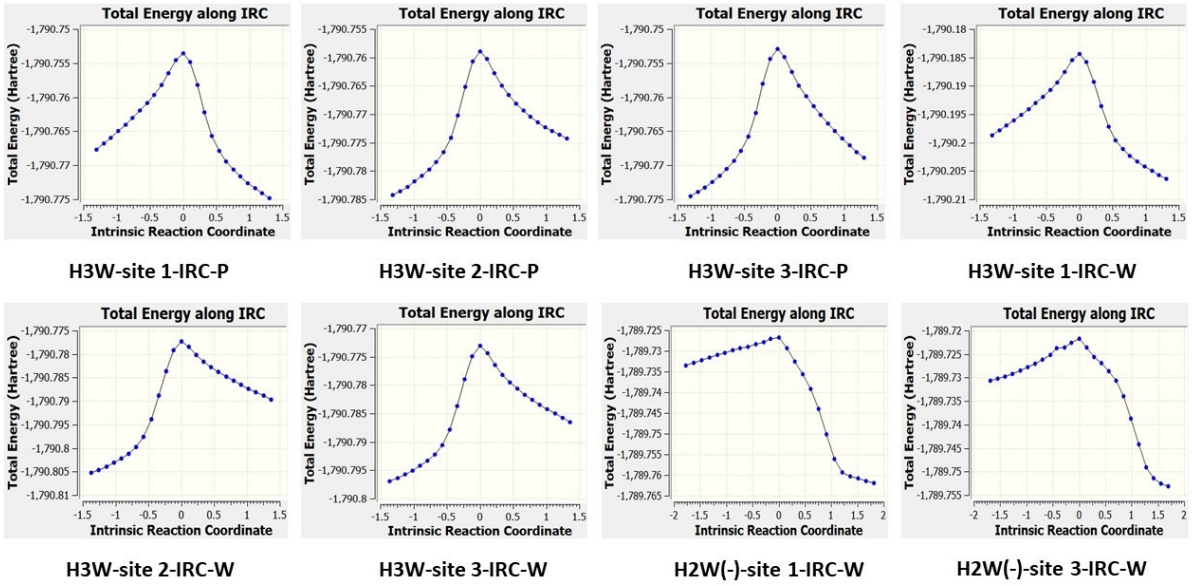

Figure S1. IRC plots for all transition states related to reaction of HOO• radical with the studied species. (W: water, P: pentylethanoate)

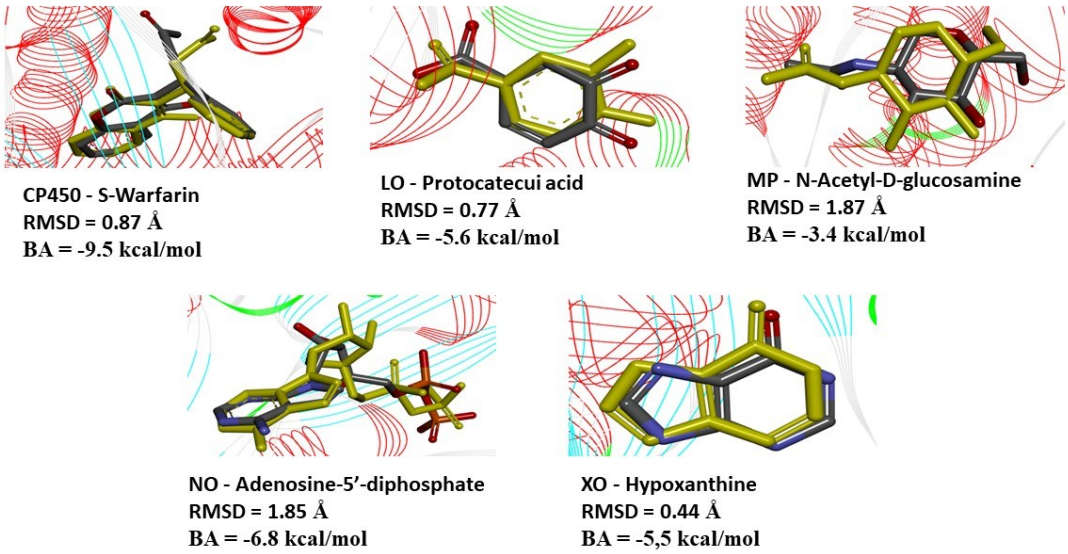

Figure S2. Parameters obtained in the validation of docking protocols for CP450, LO, MP, NO and XO receptors. The experimental structures (shown in gray) and the docked structures (shown in yellow).

References

1. M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 875-894.
2. H. Eyring, *J. Chem. Phys.*, 1935, **3**, 107-115.
3. D. G. Truhlar, W. L. Hase and J. T. Hynes, *J. Phys. Chem.*, 1983, **87**, 2664-2682.
4. T. Furuncuoglu, I. Ugur, I. Degirmenci and V. Aviyente, *Macromolecules*, 2010, **43**, 1823-1835.
5. E. Vélez, J. Quijano, R. Notario, E. Pabón, J. Murillo, J. Leal, E. Zapata and G. Alarcón, *J. Phys. Org. Chem.*, 2009, **22**, 971-977.
6. E. Pollak and P. Pechukas, *J. Am. Chem. Soc.*, 1978, **100**, 2984-2991.
7. A. Fernández-Ramos, B. A. Ellingson, R. Meana-Pañeda, J. M. Marques and D. G. Truhlar, *Theor. Chem. Acc.*, 2007, **118**, 813-826.
8. C. Eckart, *Phy. Rev.*, 1930, **35**, 1303.
9. R. A. Marcus, *Annu. Rev. Phys. Chem.*, 1964, **15**, 155-196.
10. R. A. Marcus, *Rev. Mod. Phys.*, 1993, **65**, 599.
11. Y. Lu, A. Wang, P. Shi and H. Zhang, *PloS one*, 2017, **12**, e0169773.
12. Y. Lu, A. Wang, P. Shi, H. Zhang and Z. Li, *PloS one*, 2015, **10**, e0133259.
13. S. F. Nelsen, S. C. Blackstock and Y. Kim, *J. Am. Chem. Soc.*, 1987, **109**, 677-682.
14. S. F. Nelsen, M. N. Weaver, Y. Luo, J. R. Pladziewicz, L. K. Ausman, T. L. Jentzsch and J. J. O'Konek, *J. Phys. Chem. A*, 2006, **110**, 11665-11676.
15. A. Galano and J. R. Alvarez-Idaboy, *J. Comput. Chem.*, 2013, **34**, 2430-2445.
16. F. C. Collins and G. E. Kimball, *J. Colloid Sci.* , 1949, **4**, 425-437.
17. M. Von Smoluchowski, *Z. Phys. Chem*, 1917, **92**, 129-168.
18. D. G. Truhlar, *J. Chem. Educ.*, 1985, **62**, 104.
19. A. Einstein, *Ann. Phys.*, 1905, **17**, 549-560.
20. G. G. Stokes, *Mathematical and Physical Papers*, University Press, Cambridge, 1905.
21. A. Galano and J. Raúl Alvarez-Idaboy, *Int. J. Quantum Chem.*, 2019, **119**, e25665.
22. Q. V. Vo, T. V. Gon, M. V. Bay and A. Mechler, *J. Phys. Chem. B*, 2019, **123**, 10672-10679.
23. Q. V. Vo and A. Mechler, *J. Chem. Inf. Model.*, 2020, **60**, 316-321.
24. Y. Okuno, *Chem.: Eur. J.*, 1997, **3**, 212-218.
25. S. Benson, *The foundations of chemical kinetics:* , Malabar, Florida, 1982.
26. C. Iuga, J. R. Alvarez-Idaboy and A. Vivier-Bunge, *J. Phys. Chem. B*, 2011, **115**, 12234-12246.
27. J. R. Alvarez-Idaboy, L. Reyes and N. Mora-Diez, *Org. Biomol. Chem.*, 2007, **5**, 3682-3689.
28. E. Dzib, J. L. Cabellos, F. Ortíz-Chi, S. Pan, A. Galano and G. Merino, *Int. J. Quantum Chem.*, 2019, **119**, e25686.
29. E. Dzib, J. L. Cabellos, F. Ortiz-Chi, S. Pan, A. Galano and G. Merino, *Eyringpy 1.0.2*, 2018, Cinvestav, Mérida, Yucatán.