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Research and Practice on The Molecular Design and Free Radical Scavenging Mechanism of Polyphenolic Antioxidants

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Abstract **Original Research Article**

In this paper, the polyhydroxy antioxidant molecule R was designed based on thymol and perillaldehyde. The geometric configuration of the antioxidant R molecule was optimized at the BH*and*HLYP/6-31+G(d) level using density functional theory, and frequency analysis was conducted. The calculation results show that in the process of the antioxidant molecule R reacting with hydroxyl radicals, Path V has the lowest activation energy ($\Delta G^{\neq}_{TS5}$ = 135.46 kJ·mol^{-1}), which is more advantageous from the perspective of molecular dynamics. The Relative Gibbs Free Energy of Path V is less than 0 kJ·mol^{-1}, and from the perspective of chemical thermodynamics, it can proceed spontaneously in the forward direction. This can demonstrate that Path V is the advantageous path for antioxidants to eliminate hydroxyl radicals. In this calculation, the influencing factors of temperature on the reaction mechanism were investigated. Within the range of 243K ~ 303K, the enthalpies change range of multiple reaction pathways between R molecules and hydroxyl radicals was 98.68 ~ 157.49 kJ·mol^{-1}. Moreover, with the increase of temperature, there was no significant change in the horizontal images of each pathway. The activated Gibbs Free Energy in the transition state increases slowly with the rise in temperature, and the increase in each path is basically the same, while the reaction mechanism remains unchanged. Therefore, temperature has no significant effect on the reaction mechanism of antioxidant R in eliminating hydroxyl radicals.

Keywords: Hydroxyl radical; Antioxidant molecules; Reaction mechanism; Free radical scavenging reaction.

1. INTRODUCTION

Hydroxyl radicals are one of the most destructive reactive oxygen species in living organisms, and their excessive production is closely related to many diseases. The activity of antioxidant molecules0 is mainly manifested as blocking the chain reaction of free radicals, eliminating excessive free radicals, and maintaining the REDOX balance within cells. Therefore, in the laboratory, hydroxyl radicals are used for theoretical calculations and experiments. Research on antioxidants reducing or inhibiting the production of free radicals can effectively slow down cellular aging and damage, lower the occurrence of diseases, expand the range of antioxidant choices, and provide theoretical support for inhibiting or reducing free radicals. Develop more efficient antioxidant strategies to address the challenges of oxidative stress-related diseases0.

Thymol and perillaldehyde (as shown in Fig.1(a) and (b)) are present in natural organisms and have been proven to have antioxidant properties in experimental operations0. Based on this, this paper designed a new molecule R with antioxidant activity (as shown in Fig.1(c)), attempting to study the structure-activity relationship between the molecular structure and the antioxidant capacity for scavenging hydroxyl radicals and the radical reaction pathway from a kinetic perspective, in order to determine the dominant structure and reaction mechanism for scavenging hydroxyl radicals, and to investigate the influence of temperature on the activity of hydroxyl radicals. This study provides data support for finding suitable substitutes for some substances that are difficult to extract and separate from plants, and offers a theoretical basis for mass production through chemical methods and expanding the selection range of antioxidants.

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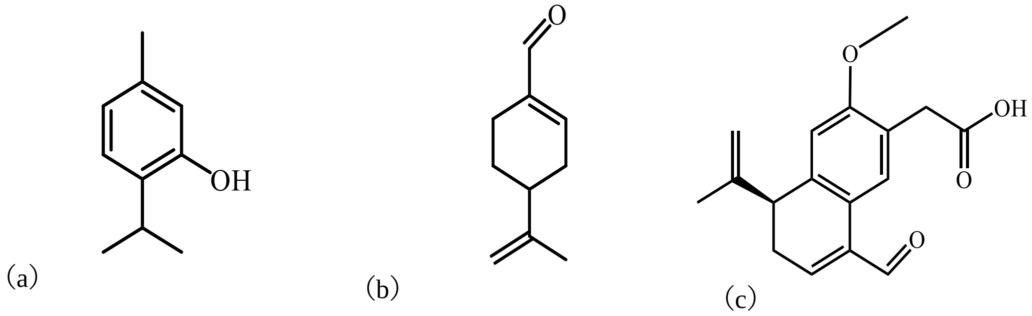

Fig.1: Thymol (a), perilla-aldehyde (b), Antioxidant molecule R(c)

2. COMPUTATIONAL METHOD

Density functional theory can be used in materials science for structural calculations to analyze the influence of vacancies or impurities in materials on electrical properties10 and the energy changes during the reaction process11. In this project, the *GaussView* software12 was used to construct a molecular model. By applying density functional theory, the geometric configuration of the C, H, and O atoms stationed on the designed antioxidant molecule (**R**) was optimized at the BH*and*HLYP/6-31+G(d) level, and frequency analysis was conducted. The simulated environmental conditions are in an ideal gas state, with a simulation temperature range of 243K to 303K. All calculations are completed in the *Gaussian Program(13)*

3. RESULT AND DISCUSSION

3.1. Structural design and optimization of Antioxidant R

Based on the experimental data of the antioxidant activity of thymol and perillaldehyde, an antioxidant molecule with an **R** structure was designed. The bond angles at each point were rotated at the BH and HLYP/6-31+G(d) level and 298 K temperature to conduct theoretical simulation calculations on this structure. The R structure was transformed by continuously adjusting factors such as bond length, bond Angle, and dihedral Angle, as shown in Table 1.

Table 1: Structure-optimized energy of antioxidant molecule R (a.u.)

Structure	***ZPVE***	***E***	***H***	***G***
R	**0.305087**	**-957.504941**	**-957.488707**	**-957.545998**
R1	0.305088	-957.504941	-957.488706	-957.545997
R2	0.305193	-957.504058	-957.487846	-957.544904
R3	0.305741	-957.497187	-957.481072	-957.537734
R4	0.304911	-957.500527	-957.484128	-957.541801
R5	0.305193	-957.5013	-957.485011	-957.542536
R6	0.304888	-957.500573	-957.484162	-957.541879
R7	0.304911	-957.500527	-957.484128	-957.541802
R8	0.305193	-957.5013	-957.485012	-957.542533
R9	0.304912	-957.500527	-957.484128	-957.541801
R10	0.305192	-957.504059	-957.487847	-957.544908
R11	0.305181	-957.504044	-957.487827	-957.544877
R12	0.304804	-957.501447	-957.485032	-957.542903

As is shown in Table 1, the physical and chemical parameters of R are as follows, *ZPVE* = 0.305087 a.u., *E* = -957.504941 a.u., *H* = -957.488707 a.u., *G* = -957.545998 a.u., whose energy value of this structure is the smallest compared with that of other structures. It is stable and represents the optimal configuration among the designed antioxidant molecular structures, as shown in Fig.2.

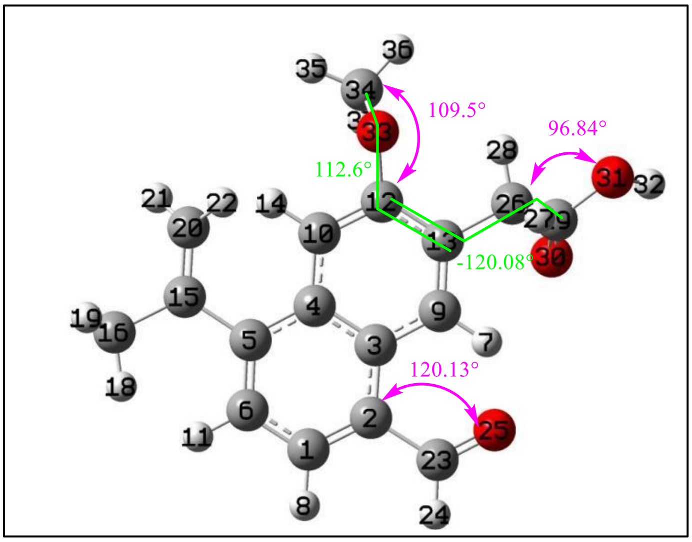

Fig. 2: Optimal structure of antioxidant molecule R

3.2 Analysis of the reaction mechanism of antioxidants in eliminating hydroxyl radicals

Based on the active sites of the substance structure, five free radical scavenging pathways were designed as shown in Fig.3. The reaction mechanism of free radical scavenging was theoretically simulated using *Gaussian 09* antioxidants. The calculation simulation results are shown in Table 2.

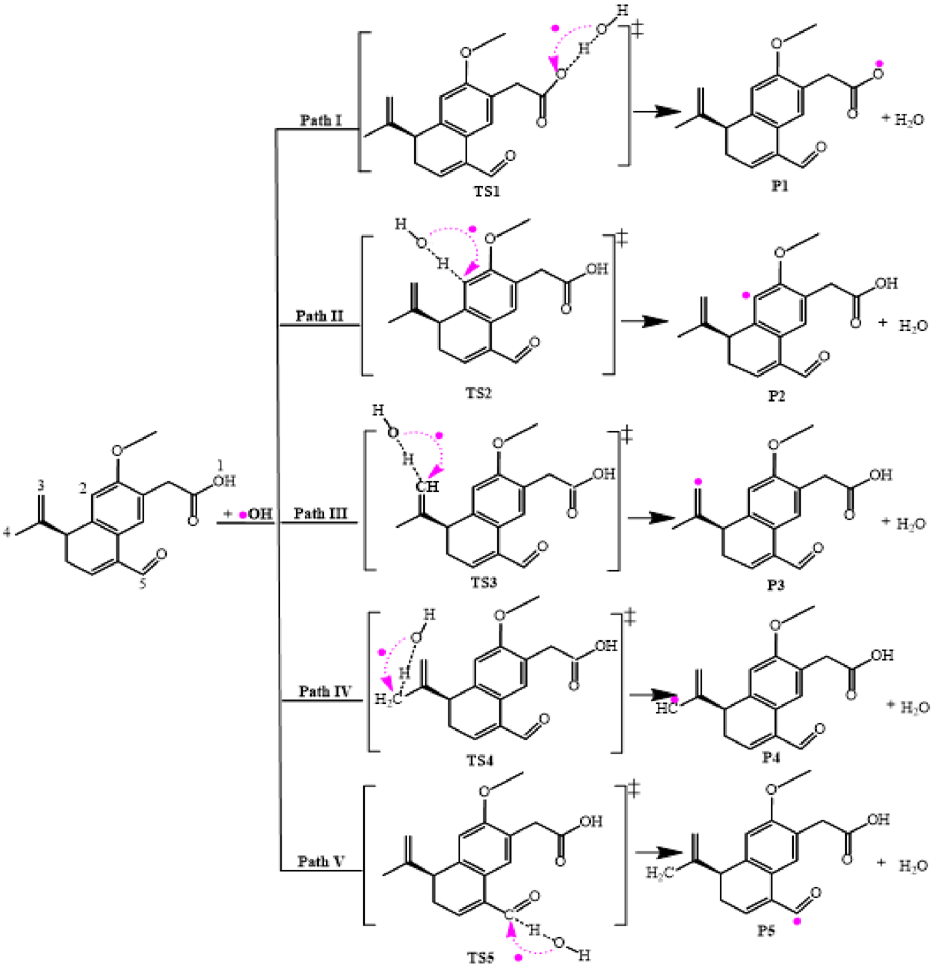

Fig.3: Design the reaction path of the antioxidant R to scavenge hydroxyl radicals

Table 2 Antioxidant molecules eliminate the energy at each site of the hydroxyl radical reaction (a.u.)

Sructure	***ZPVE***	***E***	***H***	***G***
R	0.030588	-957.50494	-957.484781	-957.553903
·OH	0.08714	-75.692397	-75.689093	-75.709313
H_2O	0.022005	-76.356678	-76.352899	-76.374301
P1	0.290864	-956.846174	-956.826009	-956.895872
P2	0.291753	-956.835731	-956.815512	-956.885626
P3	0.291175	-956.837073	-956.81686	-956.886746
P4	0.290606	-956.877428	-956.857555	-956.926778
P5	0.292192	-956.870113	-956.849954	-956.919767
TS1	0.311701	-1033.139025	-1033.117232	-1033.190073
TS2	0.311474	-1033.136298	-1033.113893	-1033.188281
TS3	0.311439	-1033.142092	-1033.119637	-1033.194813
TS4	0.312202	-1033.152993	-1033.131033	-1033.204823
TS5	0.312581	-1033.158699	-1033.136287	-1033.211622

P1 ~ P5 is a new free radical produced after the hydroxyl radical attacks the antioxidant molecule R. In the reaction where antioxidant molecules eliminate hydroxyl radicals, the physical and chemical parameters of P4 are the smallest, and their corresponding energies are E = -956.877428 a.u., H = -956.857555 a.u. and G = -956.926778 a.u. respectively. The level of Gibbs Free Energy can reflect the thermodynamic stability of a system. A lower Gibbs Free Energy indicates that the system is in a stable state. Therefore, based on Gibbs Free Energy, P4 is the most stable product, the free radical.

TS1~TS5 is the transition state after the hydroxyl radical attacks the antioxidant molecule R. During the process of antioxidant molecules eliminating hydroxyl radicals, the transition state energy of TS5 is the smallest, and its physical and chemical parameters are $\Delta E^{\neq}_{TS5}$ = -1033.158699 a.u., $\Delta H^{\neq}_{TS5}$ = -1033.136287 a.u. and $\Delta G^{\neq}_{TS5}$ = -1033.211622 a.u. respectively.

Based on Tables 2 the above formulas, the five energy barrier diagrams of antioxidant molecules scavenging free radicals at 298K as shown in Fig.4 were plotted.

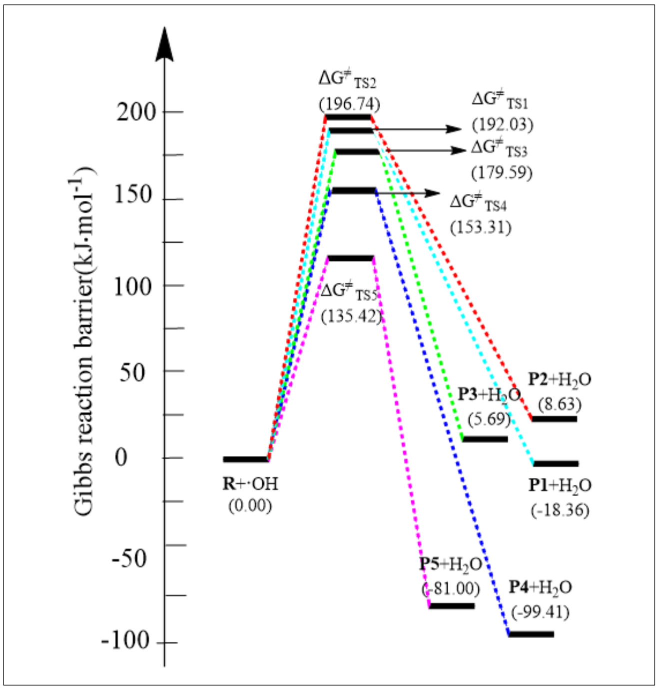

Fig. 4: The reaction barrier of hydroxyl radical scavenging by 298K antioxidants

Fig.4 describes the changes in the activated Gibbs Free Energy of the reaction transition state in five paths. It can be seen from the figure that the reaction pathway has multiple branches near the starting point, indicating that hydroxyl radicals can attack multiple different positions on the antioxidant molecule. These branches correspond to multiple active sites in the antioxidant molecular structure, which can interact with hydroxyl radicals. Each path presents a different energy barrier height. The higher the energy barrier, the greater the energy obstacle the path needs to overcome, the more difficult the reaction is to proceed, and the reaction rate is usually slower. Conversely, pathways with lower energy barriers are more likely to undergo reactions and have a faster reaction rate. By comparing the levels of energy barriers, the dominant pathways for antioxidant molecules to clear hydroxyl radicals can be determined. It can be seen from the figure that the energy barrier of Path V is the lowest, and the activated Gibbs Free Energy of the reactive transition state is the smallest. The activated Gibbs Free Energy of Path V is $\Delta G^{\neq}_{TS5}$ = 135.37 kJ·mol^{-1}, which differs from that of the transition states corresponding to Path I, Path II, Path III, and Path IV by 56.58 kJ·mol^{-1}, 61.28 kJ·mol^{-1}, 44.13 kJ·mol^{-1} and 17.85 kJ·mol^{-1}.

Based on the data of the Gibbs Free Energy change of the reaction, the best Path attacked by the hydroxyl radical is Path IV, with the Gibbs Free Energy of the reaction being $\Delta_r G_{Path\ IV}$ = -99.41 kJ·mol^{-1}. However, the substitution reaction of the diatom makes the transition state intermediate a rate-determining step. Compared with Path V, the transition state activation Gibbs Free Energy of Path IV is higher and less likely to react, while the reaction Gibbs Free Energy of Path V is $\Delta_r G_{Path\ V}$ = -81.00 kJ·mol^{-1}. Therefore, Path V remains the best path for hydroxyl radicals to attack antioxidant molecules. Considering the transition state energy and product energy comprehensively, the Path reaction of Path V is easier than other paths and is in a thermodynamically favorable direction. This figure provides an important theoretical basis for understanding the mechanism of action of antioxidants by showing the changes in the activation Gibbs free energy of the reaction pathways of hydroxyl radicals attacking different positions of the antioxidant molecule under the same structure when antioxidant molecules eliminate hydroxyl radicals.

3.3 Analysis of the influence of Temperature on the reaction mechanism of Antioxidant scavenging of hydroxyl radicals

By analyzing the molecular structure property parameter data, thermodynamic and kinetic data of the reaction mechanism, and information data such as the optimal reaction path obtained from the simulation, the influence of hydroxyl sites and temperature on biological activity was studied, and the frequency of hydroxyl radical scavenging at all sites of the antioxidant within the range of 243K to 303K was calculated. The activation enthalpy changes and the activation Gibbs free energy change of the antioxidant at different temperatures were obtained, as shown in Fig.5 and Fig.6.

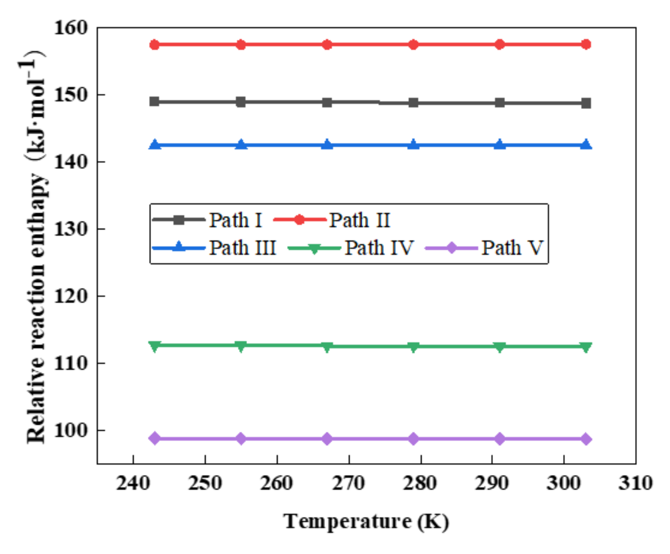

Fig. 5: The activation enthalpy changes of antioxidant scavenging hydroxyl free radicals at different temperatures

As shown in Fig.5, the enthalpies change of the antioxidant molecule R in scavenging hydroxyl radicals at different temperatures ranging from 243K to 303K is described. It can be clearly observed from the figure that the activation enthalpy of each Path from Path I to Path V remains basically consistent at the level without obvious fluctuations. Path I fluctuates within the range of 148.69 ~ 148.97 kJ·mol^{-1}, Path II fluctuates within the range of 157.41 ~ 157.49kJ·mol^{-1}, Path III fluctuates within the range of 142.37 ~ 142.42 kJ·mol^{-1}, Path IV fluctuates within the range of 112.47~112.65 kJ·mol^{-1}, and Path V fluctuates within the range of 98.68~98.76 kJ·mol^{-1}. Moreover, with the increase of temperature, there is no obvious fluctuation change in the image. Thus, it can be concluded that Temperature has little effect on the reaction enthalpy of antioxidant molecules in eliminating hydroxyl radicals.

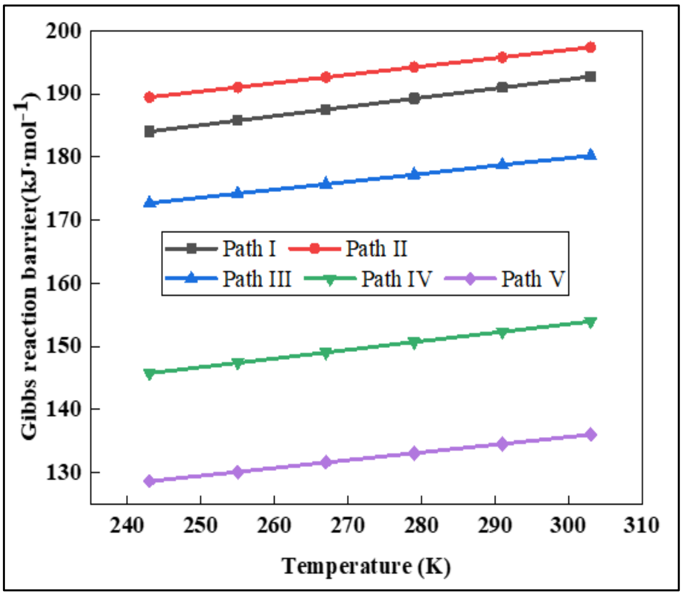

Fig. 6: The Gibbs Free Energy of activation of antioxidant reaction to remove hydroxyl radical at different temperatures

It can be seen from the figure that the pathways of each antioxidant molecule's free radical scavenging reaction increase slowly with the rise of temperature. Each pathway rises within a certain range, and Path I fluctuates within the range of 184.04 ~ 192.74 kJ·mol^{-1}. Path II fluctuates within the range of 189.47 ~ 197.38 kJ·mol^{-1}, Path III fluctuates within the range of 172.71 ~ 180.20 kJ·mol^{-1}, Path IV fluctuates within the range of 145.75 ~ 153.98 kJ·mol^{-1}. and Path V fluctuates within the range of 128.66 ~ 136.04 kJ·mol^{-1}, and the increase amplitude of each path is basically the same. It can be concluded from this that the dominant pathway by which antioxidants clear free radicals has not changed, and there is no impact on the reaction mechanism by which antioxidants clear hydroxyl radicals.

4 CONCLUSIONS

In this paper, multiple pathways of the reaction between reactant R and hydroxyl radicals were designed and simulated. The influence of temperature on the reaction mechanism was explained from both kinetic and thermodynamic perspectives. The conclusions are as follows:

1. Among the design of antioxidant molecules, the R structure is the most stable, whose Gibbs Free Energy is -957.553903 a.u. and the lowest enthalpy is -957.484781 a.u..
2. Comprehensively considering the reactive Gibbs Free Energy of antioxidant scavenging hydroxyl radicals and the transition state activation Gibbs free energy change, the transition state energy ($\Delta G^{\neq}_{\mathrm{TS5}}$ = 135.46 kJ·mol^{-1}) of Path V is in a favorable kinetic direction, and the reactive Gibbs Free Energy change ($\Delta_r G_{\mathrm{Path\ V}}$ = -81 kJ·mol^{-1}) is thermodynamically spontaneous in a positive direction. Therefore, the dominant pathway for antioxidants to clear hydroxyl radicals is Path V.
3. In the study of the influence of temperature on the scavenging of hydroxyl radicals by antioxidants, it was observed that the activation enthalpy change of the transition state did not change significantly with the increase in temperature, while the activation Gibbs free energy change of the transition state increased slowly with the rise in temperature, and the increase in each path was basically the same. Therefore, from the activation enthalpy change and the activation Gibbs free energy change, it can be known that Changes in temperature do not cause alterations in the reaction mechanism by which antioxidants clear hydroxyl radicals.

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REFERENCES

1. LI Xiyou, GU Xiaoyuan, MAO Jianghao, *et al.*, In vivo and in vitro antioxidant activity detection methods[J]. Chemistry of Life, 2024, 44(05):853-862.

2. Vinita Sindhi, Vartika Gupta, Kameshwar Sharma, *et al.*, Potential applications of antioxidants A review[J], Journal of Pharmacy Research, 2013, 7 (9): 828-835
3. Zhang Deli, Huang Yingping, Luo Guangfu, *et al.*, Research Progress of Fenton and Photo-Fenton Reactions[J]. Environmental Chemistry, 2006, 25(2): 121-127.
4. C C W. Reconciling the chemistry and biology of reactive oxygen species. [J]. Nature chemical biology,2008,4(5):278-86.
5. GUAN Li, WEI Wen-zhi, YU Dan-dan, *et al.*, Study on Bioactive Components and Antioxidant Activity of Different Varieties of Perilla frutescens Juice[J]. China Condiment, 2024, 49(11): 42-47.
6. LI Meng-hao, ZHAO Ya-na, LI Hui-zhen, *et al.*, Study on Preparation and Antioxidant Activity of Perilla Flavor V inegar[J]. China Condiment, 2023, 48(04): 29-36.
7. LIU Min, YU Xiong-ying, SHU Qing-long, *et al.*, The antioxidant and antityrosinase activities of thymol[J]. Journal of Li-shizhen Traditional Chinese, 2018, 29(02): 274-277.
8. Nikolaos Nenadis, Maria Z. Tsimidou, Contribution of DFT computed molecular descriptors in the study of radical scavenging activity trend of natural hydroxybenzaldehydes and corresponding acids[J], Food Research Internationa, 2012, 48 (2): 538-543.
9. YANG Fang, WANG Hai-feng. Density Functional Theory Calculation of Four Kinds of Nitrogen-containing Resveratrol Derivatives[J]. Guangzhou Chemical Industry, 2019, 47(05): 84-87.
10. Anubhav Jain, Shyue Ping Ong, Geoffroy Hautier, *et al.*, Commentary: The Materials Project: A materials genome approach to accelerating materials innovation[J]. APL Materials, 2013, 1 (1):011002-011002.
11. Nadim E, Paraskar P, Moradi H, *et al.*, Kinetic and thermodynamic analysis of hemp oil epoxidation with density functional theory insights into unsaturated fatty acid epoxidation and ring-opening reactions[J]. Chemical Engineering Journal Advances,2025,22(2025):100749-100749.
12. Ding Degang, Liu Zhijing, Xu Jun. Application of Chemoffice19 Combined with Gauss view 5.0 in the Visual Teaching of Organic Chemistry[J]. Shandong Chemical Industry, 2020, 49(23): 213-214.
13. Yali Tian. A study on the application of Gaussian 09 and Gauss View 5.0 software in visual chemistry teaching in middle schools [D]. Shaanxi Normal University, 2015.