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DENSITY FUNCTIONAL THEORY STUDY ON THE CRYSTAL STRUCTURE OF QUERCETIN

Jie Li[1], Junlong Wang[2], Jiajun Cui[1], Hongchen Du[3], Rongkai Pan[3], Xiqing Dong[3], Yuzhen Niu[3], Lijuan Feng[3], Jingyi Du[4] and Weiwei Huan[1*]

[1]College of Chemistry and Materials Engineering, Zhejiang A&F University, Hangzhou 311300, China
[2]College of Food and Health, Zhejiang A&F University, Hangzhou, Zhejiang 311300, China
[3]Shandong Engineering Research Center of Green and High-Value Marine Fine Chemical, Weifang University of Science and Technology, Weifang 262700, China
[4]School of Literature, History and Culture, Qilu Normal University, Jinan 250013, China

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ABSTRACT. A molecular mechanics method with COMPASS and Dreiding force fields were used to predict molecular packings for quercetin (P21/c, P212121, P-1, Pbca, C2/c, Pna21, and P21). According to the minimum energy principle, the most likely crystal accumulation mode of quercetin belongs to P-1. Then, periodic band calculations were performed on the predicted crystals using the density functional theory generalized gradient approximation with revised Perdew-Burke-Ernzerhof (DFT-GGA-RPBE) functional method. LUCO (the lowest unoccupied crystal orbital) is mainly contributed by the p-state of the C atom, while HOCO (the highest occupied crystal orbital) is mainly composed of the p-states of the O atom.

KEY WORDS: Crystal structure, Quercetin, Theoretical study

INTRODUCTION

Flavonoids are a class of polyphenolic secondary metabolites which are widely found in plants and diets. Flavonoids have a structural backbone of 15 carbon atoms, consisting of two benzene rings (A and B) and a heterocycle (C). This carbon skeleton structure can be abbreviated as C6-C3-C6. Depending on the structure of the C-ring, they can be classified into various structural classifications such as flavonoids, flavonols, chalcones, isoflavonoids, anthocyanins, biflavonoids, and so on. The difference between the different structural classifications varies in the oxidation level and substitution position of the C-ring. Flavonoids have a variety of biological activities, including antioxidant activity, free radical scavenging activity, prevention of coronary heart disease, hepatoprotective activity, anti-inflammatory and anticancer activity, while some flavonoids also have potential antiviral activity [1-4].

Mistercetin, also known as mistercetin and quercetin, is a kind of plant flavonol, belonging to the flavonoid of polyphenols, which is found in fruits, vegetables, grains and other plants. Quercetin and its derivatives are the most widely distributed flavonoids in the plant world compounds rich in mango, apple, pear, grape, cherry, tea, spring onion, carrots and red wine.

Based on the previous studies, due to lack of data of the crystal structure of quercetin, the present study will be useful to evaluate the properties of quercetin.

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*Corresponding authors. E-mail: huanweiwei@zafu.edu.cn

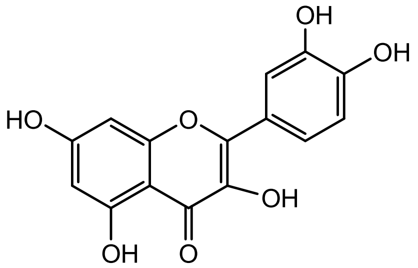


Figure 1. Molecular structure of quercetin.

CALCULATION METHODS

The B3LYP function combined with the 6-311++g(d,p) basis set is used for geometric optimization and frequency calculation [5, 6]. All calculations are implemented using the Gaussian09 package [7].

Due to the large size of the molecules of the title compound and too many possible packings in different space groups, empirical force field is more suitable for finding molecular packing than quantum mechanics, so it is important to choose a suitable force field type.

As is known, among the 230 space groups, over 80% organic crystals belong to 7 typical space groups based on the statistical data, which are $P2_1/c$, $P2_12_12_1$, P-1, Pbca, C2/c, Pna2_1 and $P2_1$ [8-12], the chosen force field method is then used to do a global search in the above 7 space groups, and finally 7 most stable polymorphs are obtained, the polymorph with the lowest energy will be recommended as the reasonable crystal from.

Based on the periodic bound condition, theoretical calculations on a crystal at atomic level can effectively simulate its physical and chemical properties. The GGA-RPBE (Generalized Gradient Approximation with Revised Perdew–Burke–Ernzerhof functional) method in CASTEP code based on the DFT was performed to calculate the band structure and density of states (DOS).

RESULTS AND DISCUSSION

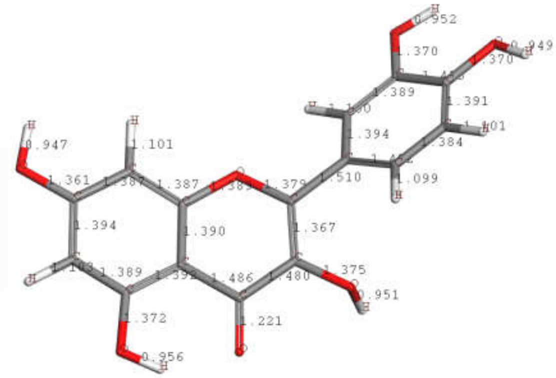
The choice of force field

Both COMPASS and Dreiding are useful molecular force fields with distinct characteristics and areas of application. COMPASS is more comprehensive and accurate for a wider range of materials, while Dreiding is more general and versatile for inorganic compounds.

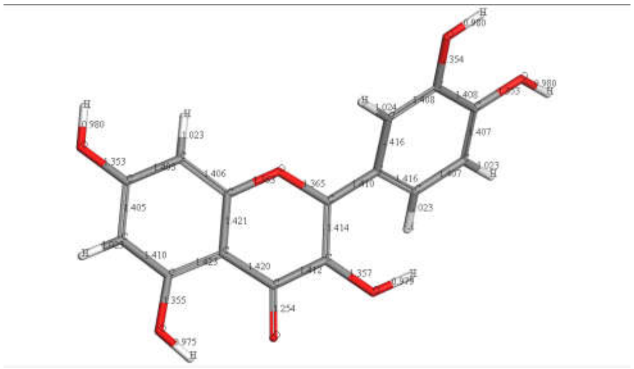
Figure 2 shows the calculated structures based on Compass, Dreiding and B3LYP/6-311++g(d,p), we can see that the results from Compass are more stable, for example, the bond length of carbanyl group from Compass, Dreiding and DFT are 1.221 Å, 1.254 Å and 1.242 Å, respectively, so the bond length from Compass force field is more stable, because the smaller the bond length, the more stable it is, therefore, the Compass force field was used to predict the molecular packing forms of the title compound.

The energy (E), cell parameters (a, b, c, α, β, γ), and density (ρ) of the most probable crystal structures predicted by Compass force field method are shown in Table 1. It can be seen that different forms of filler have different energies and densities, and the energy of various fillers calculated by force field is between -98.48 ~ -95.33 kcal mol^{-1} cell^{-1}. Depending on the principle that possible stable crystals usually have lower energies, the crystal structure of quercetin is more likely to belong to the P-1 group. The crystal structure is further optimized with DFT.

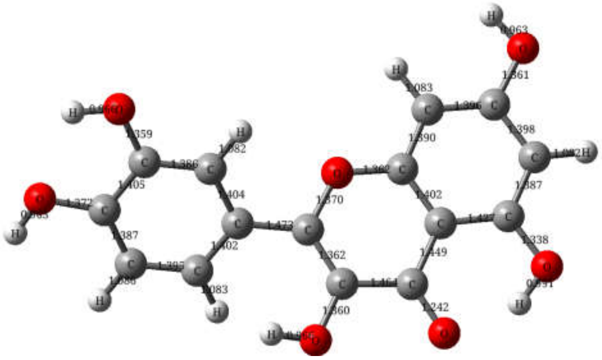
The selected crystal structure was further optimized by DFT-GGA method (Figure 3). The equilibrium structure of the heading compound is obtained by the complete relaxation of the cell parameters allowed by P-1 crystal symmetry and the atomic position inside the cell.



Compass



Dreding



B3LYP

Figure 2. Optimized molecular structures and parameters (bond lengths in angstrom).

Table 1 lists the parameters from Compass force field, we can see that, according to the principle the most possible polymorph usually possesses lower energy, it can be concluded that quercetin tends to crystalline in *P*-1 from Compass force field. Calculated results are consistent with previous literature reports [13-15].

The density functional theory method DFT-GGA-RPBE was then performed to optimize the predicted packing (Figure 3), the corresponding cell parameters are a = 18.95 Å, b = 15.13 Å, c = 18.55 Å, α = 42.20º, β = 87.23º, γ = 46.32º.

Table 1. Possible molecular packings in seven most possible space groups from the Compass force field.

Space groups	$P2_1/c$	$P2_12_12_1$	P-1	Pbca	$C2$/c	Pna2_1	**$P2_1$**
Z	4	4	2	8	8	4	2
E/ kcal/mol/asym cell	-97.71	-98.14	-98.48	-97.76	-95.33	-95.86	-96.65
a/ Å	3.81	12.47	7.68	25.54	23.47	15.96	6.94
b/ Å	29.75	3.83	12.28	6.75	6.91	6.83	11.04
c/ Å	11.39	24.00	14.40	13.49	16.58	11.09	8.45
α/ º	90.00	90.00	81.90	90.00	90.00	90.00	90.00
β/ º	65.76	90.00	28.76	90.00	77.71	90.00	68.25
γ/ º	90.00	90.00	90.70	90.00	90.00	90.00	90.00
ρ/ g•cm^{-3}	1.70	1.75	1.62	1.73	1.53	1.66	1.67

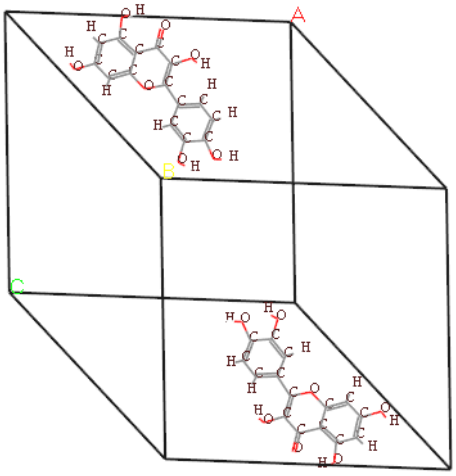


Figure 3. The optimized crystal structure of quercetin using DFT-GGA-RPBE in *P-1* space group.

Band gap

Periodic band calculations, or band structure calculations, are of significant importance in the fields of solid-state physics, materials science, and chemical physics. These calculations provide a deep understanding of the electronic properties of crystalline materials. Periodic band calculations allow researchers to determine the energy levels and dispersion relations of electrons in a crystalline solid. This information is crucial for understanding how electrons move through the material and interact with other particles.

Periodic band calculations are a powerful tool for understanding the electronic properties of crystalline materials and predicting their various physical and chemical properties. These calculations have important implications for material design, discovery, and the development of new technologies across a wide range of fields.

The band gap is an important parameter used to characterize the electronic structure of crystals and generally refers to the energy difference in electron volts between the top of the insulator and semiconductor medium valence band (HOCO) and the bottom of the conduction band (LUCO). This is equivalent to releasing a shell electron from its orbit around the nucleus as the energy required to move the charge carrier, which moves freely within the solid material. Compounds with a large band gap are generally insulators and semiconductors with a small band gap, while conductors are either very small or not, as valence bands and conductors overlap. It is related to impact sensitivity and can be used as a standard for predicting the sensitivity of high energy materials with similar structures. According to the equilibrium crystal structure of the leading compound obtained at the level of GGA-RPBE, the self-synchronous structure of different symmetry directions in the Brillouin range is calculated and analysed. The GGA-RPBE functional has been widely used in studies of diverse materials, including oxides, nitrides, and metal-organic frameworks. Its applicability to a wide range of systems makes it a versatile tool for researchers working in different areas of solid-state physics and materials science. In summary, periodic band calculations are essential for understanding the electronic properties of crystalline materials and guiding the design and discovery of new materials. The GGA-RPBE functional is a popular choice for these calculations due to its balance between accuracy and computational efficiency, making it a versatile tool for researchers in the field.

Density of state is a presentation of the band structure of a crystal. A better understanding of the band structure is its partial DOS (PDOS), in which the DOS is projected on the atom-centered orbital, and PDOS can be used to investigate the constitution of energy bands.

In general, the band gap (ΔE_g) between the highest occupied crystal orbital and the lowest unoccupied crystal orbital can be used as a criterion to predict the sensitivity of energetic materials with similar structures, and the smaller the ΔE_g, the easier the electron transits and the greater the sensitivity will be. This principle has been illustrated by many experimental results and is useful both for ionic crystals and molecular crystals.

Figure 4 shows the band structure of quercetin, the band gap is 1.667 eV, which is similar with another flavonoid compound myricetin and indicates that it is a semiconductor.

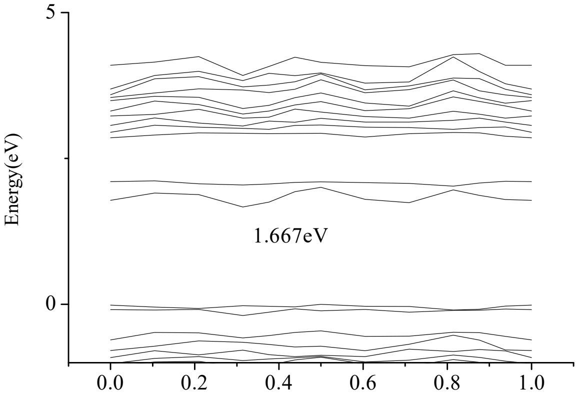


Figure 4. The energy bands at ambient pressure along the different symmetric direction of the Brillouin zone.

Density of states

In order to obtain more information about the bonding nature of the title compounds, the total electronic density of states and the partial DOS (PDOS) are calculated and shown in Figure 5. The density of states (DOS) is a representation of the band structure of a crystal and can reveal the composition of the valence band (HOCO) and the conduction band (LUCO). A better understanding of the band structure is provided by the Partial Density of States (PDOS), where the DOS is projected onto the atom-centred orbital and can be used to investigate the constitution of the energy bands. From Figure 5 it can be seen that the DOS are finite at the Fermi level because the DOS contain some form of broadening effect. In the upper valence bands, the title compounds have a sharp peak near the Fermi level, indicating that the upper valence band of the band structures are flat, all peaks are predominantly from the p states. In addition, several main peaks in the upper valence band are superimposed by the s and p states. The conduction bands are also dominated by the p states, indicating that the p states play an important role in their chemical reaction.

Analysing the DOS and PDOS of the crystal structures with P-1 symmetry is shown in Figure 5, it can be seen that in quercetin LUCO is mainly contributed by the p-state of the C atom, while HOCO is mainly composed of the p-states of the O atom.

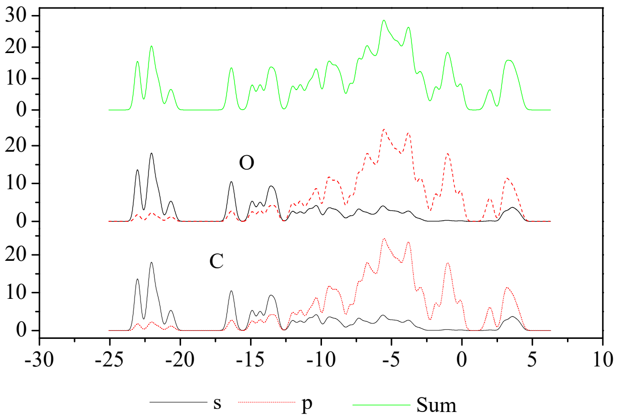


Figure 5. Total DOS (TDOS) and partial DOS (PDOS).

CONCLUSIONS

In this study, the crystal structure of quercetin was studied using theoretical calculation. According to the minimum energy principle, the most likely crystal accumulation mode of quercetin belongs to P-1. The calculated band gap is 1.667 eV, which is similar with another flavonoid compound myricetin and indicates that it is a semiconductor. LUCO (The lowest unoccupied crystal orbital) is mainly contributed by the p-state of the C atom, while HOCO (The highest occupied crystal orbital) is mainly composed of the p-states of the O atom.

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Authors contribution

The first two authors contributed equally to this work.

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