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Degradation reactions of Covid-19 active ingredients by molecular modeling method

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The coronavirus (Covid) is a large family of viruses known to cause a variety of illnesses, from the common cold to acute respiratory infections. The severity of the infection can be seen as pneumonia, acute respiratory syndrome and even death. This group of viruses was largely ignored until the SARS epidemic. However, since the SARS and MERS outbreaks, these viruses have been studied in more detail to advance vaccine research. On December 31, 2019, mysterious cases of pneumonia were detected in the city of Wuhan in China's Hubei Province. On January 7, 2020, the cause was identified as a novel coronavirus (2019-nCovid), and the disease was later named Covid-19 by WHO. In this study, possible reaction pathways of Afzelin, Delta Viniferin and Hesperidin molecules between OH radical were determined. Optimized geometries were plotted with Gauss View 5. Then, the lowest energy states were found by geometric optimization with the Gaussian 09 program.

Keywords: Covid-19, DFT, OH radical, Gaussian 09W

INTRODUCTION

Coronavirus is a family of viruses with a positive-sense RNA that possess an outer viral coat. When looked at with the help of an electron microscope, there appears to be a unique corona around it. This family of viruses mainly cause respiratory diseases in humans, in the forms of common cold or pneumonia, as well as respiratory infections. These viruses can infect animals as well [1-2].

Up to the year 2003, coronavirus (CoV) had attracted limited interest from researchers. However, after the SARS (severe acute respiratory syndrome) outbreak caused by the SARS-CoV, the coronavirus was looked at with renewed interest [3, 4]. This also happened to be the first epidemic of the 21st century originating in the Guangdong province of China. Almost 10 years later, there was a MERS (Middle East respiratory syndrome) outbreak in 2012, which was caused by the MERS-CoV [5, 6]. Both SARS and MERS have a zoonotic origin and originated from bats. A unique feature of these viruses is the ability to mutate rapidly and adapt to a new host.

Coronaviruses are known to use Keni *et al.* COVID-19: a summary the angiotensin-converting enzyme-2 (ACE-2) receptor or the dipeptidyl peptidase IV (DPP-4) protein to gain entry into cells for replication [7-10].

In this study, geometric optimizations of reactions will be made on the basis of the DFT/B3LYP/6-31G(d) (Becke(B) 3 Lee-Yang-Parr (LYP)) method of quantum mechanical density functional theory (DFT). Fragmentation reaction mechanisms will be elucidated by using the calculated energy values for each molecule. All calculations of the active ingredients of Covid-19 will be performed both in the gas phase and in the water phase by modeling the solvent effect.

Active ingredients of Covid-19 are Afzelin, Delta Viniferin, and Hesperidin. Molecular weights and molecular formulas of Covid-19 active ingredients are given in Table 1.

Table 1. Molecular weights and molecular formulas of Covid-19 active ingredients

	Afzelin	Delta Viniferin	Hesperidin
Molecular weight	432.4 g/mol	454.5 g/mol	610.6 g/mol
Molecular formula	$C_{21}H_{20}O_{10}$	$C_{28}H_{22}O_6$	$C_{28}H_{34}O_{15}$

METHODOLOGY

The reaction model used in the computational part of this study is the reaction between the afzelin, delta viniferin, hesperidin molecules and the photo-generated •OH radicals [11]. Therefore, all the calculations were based on hydroxyl radical chemistry. Hydroxyl radicals can react with organic compounds by (i) hydrogen abstraction from single bonds, (ii) addition to double bonds, and (iii) one-electron oxidation, which is mostly loss of water from hydroxyl radical adducts. The reaction system under consideration consists of •OH radicals, in other words, open-shell species. It is well known that open-shell molecules pose severe problems in quantum mechanical calculations. Hartree–Fock (HF) methods suffer from spin contamination, because they are wave function-based. In contrast to

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the HF methods, density functional theory (DFT) methods use the exact electron density instead of the wave function to calculate molecular properties and energies. Electron correlation, whose absence is the main drawback to HF methods, is accounted for in DFT methods. They suffer from spin contamination less than HF methods and this feature makes them suitable for calculations involving open-shell systems. Therefore, geometry optimizations of the reactants were performed with the DFT method. The DFT calculations were carried out as implemented in GAUSSIAN 09 code [12], using the exchange-correlation functional B3LYP, which combines HF and Becke exchange terms with the Lee–Yang–Parr correlation functional, in combination with the 6-31G* basis set. Vibrational frequencies were calculated for the determination of the structures as stationary points and true minima on the potential energy surfaces. All the possible stationary geometries located as minima were generated by free rotation around single bonds [13].

RESULTS AND DISCUSSION

Theoretical prediction of the degradation mechanism

In the search for a plausible mechanism for the photocatalytic degradation reaction of Afzelin, Delta Viniferin and Hesperidin molecules DFT reactivity descriptors were employed to have information about the most susceptible sites for hydroxyl radical attack. Fig. 1 shows the optimized structure of Afzelin, Delta Viniferin and Hesperidin molecules and the numbering system that is used throughout the calculations. Three main competing reaction pathways shown in Fig. 2 were determined by selecting the specific sites of Afzelin molecule, on the basis of their softness values being close to that of the •OH radical.

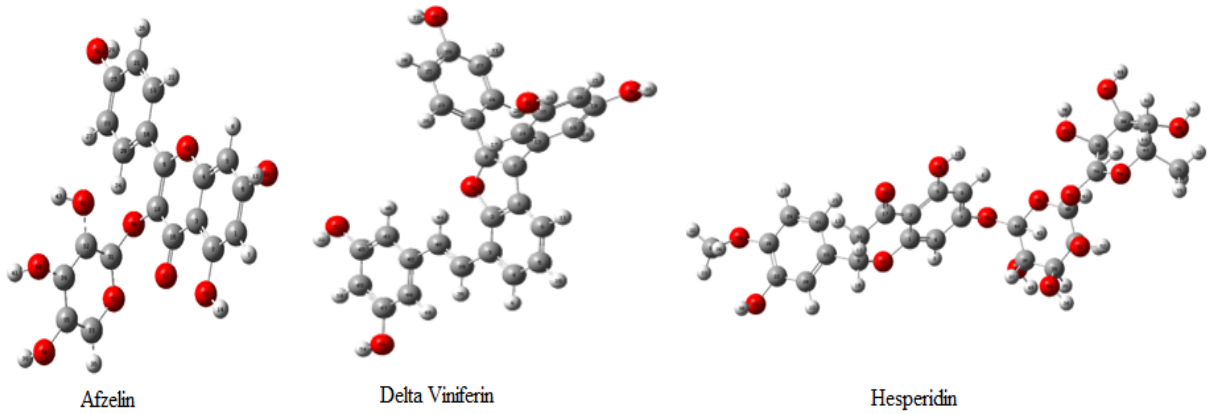

Fig. 1. Optimized geometric structure of Afzelin, Delta Viniferin and Hesperidin molecules *via* DFT method. (grey, C; white, H; red, O).

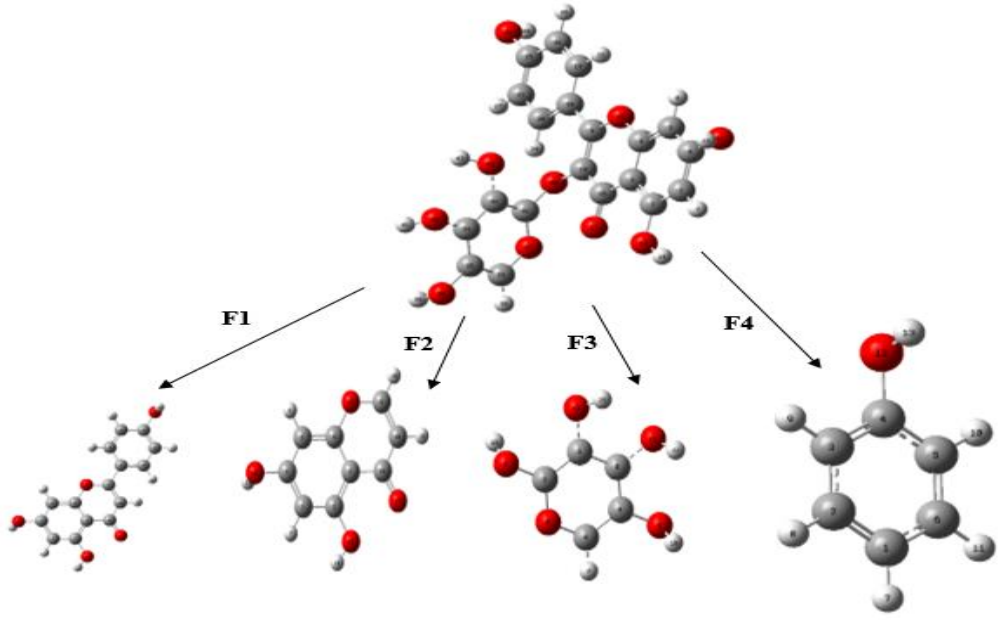

Fig. 2. Possible pathways for the photocatalytic degradation of Afzelin (grey, C; white, H; red, O)

Table 2. Constant energy, enthalpy and Gibbs free energy values according to the DFT method.

Molecules	Phase	Energy (kcal mol^{-1})	Enthalpy (kcal mol^{-1})	Gibbs free energy (kcal mol^{-1})
Afzelin	Gas	-954891.659	-954891.069	-954945.487
	COSMO	-954912.963	-954912.373	-954966.590
F1	Gas	-598315.296	-598314.704	-598353.105
	COSMO	-598330.741	-598330.149	-598368.530
F2	Gas	-406179.408	-406178.815	-406207.980
	COSMO	-406191.317	-406190.724	-406219.706
F3	Gas	-357324.236	-357323.643	-357353.844
	COSMO	-357331.972	-357331.379	-357361.547
F4	Gas	-192819.296	-192818.703	-192840.874
	COSMO	-192871.883	-192871.290	-192893.531

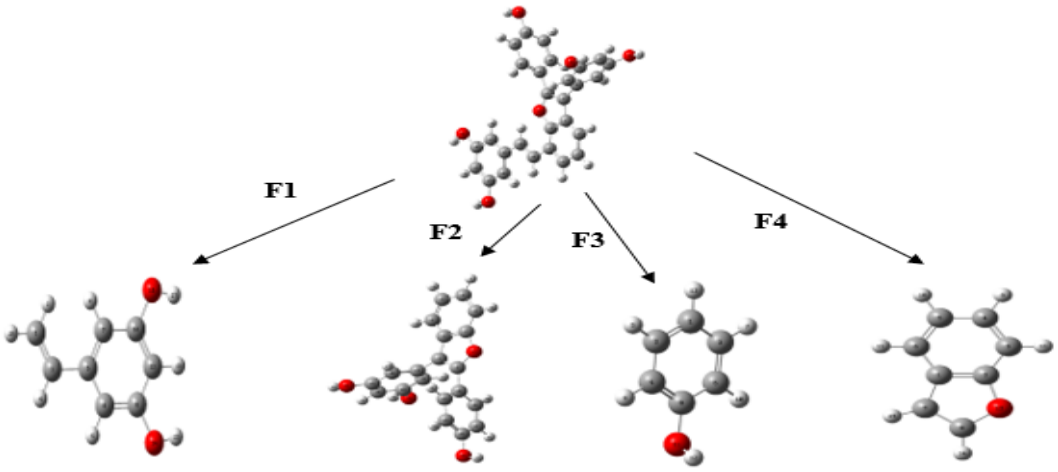

Fig. 3. Possible pathways for the photocatalytic degradation of Delta Viniferin (grey, C; white, H; red, O)

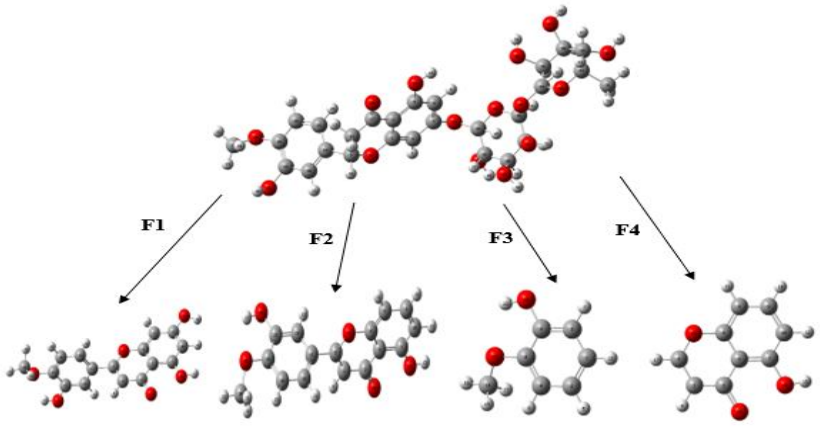

Fig. 4. Possible pathways for the photocatalytic degradation of Hesperidin (grey, C; white, H; red, O)

Table 3. Constant energy, enthalpy and Gibbs free energy values according to the DFT method.

Molecules	Phase	Energy (kcal mol^{-1})	Enthalpy (kcal mol^{-1})	Gibbs free energy (kcal mol^{-1})
Delta Viniferin	Gas	-960021.093	-960020.503	-960078.234
	COSMO	-960039.297	-960038.701	-960096.714
F1	Gas	-288609.624	-288609.031	-288636.960
	COSMO	-288616.978	-288616.385	-288644.319
F2	Gas	-672144.010	-672143.420	-672186.310
	COSMO	-672155.443	-672154.847	-672197.650
F3	Gas	-192867.756	-192867.164	-192889.392
	COSMO	-192871.884	-192871.291	-192893.531
F4	Gas	-240680.946	-240680.353	-240703.587
	COSMO	-240683.436	-240682.844	-240706.083

Table 4. Constant energy, enthalpy and Gibbs free energy values according to the DFT method.

Molecules	Phase	Energy (kcal mol^{-1})	Enthalpy (kcal mol^{-1})	Gibbs free energy (kcal mol^{-1})
Hesperidin	Gas	-1365293.170	-1365292.580	-1365365.410
	COSMO	-1365322.340	-1365321.740	-1365393.890
F1	Gas	-670157.649	-670157.053	-670199.215
	COSMO	-670173.036	-670172.446	-670214.558
F2	Gas	-622961.753	-622961.161	-623001.670
	COSMO	-622974.269	-622973.676	-623014.129
F3	Gas	-264710.265	-264709.673	-264735.726
	COSMO	-264714.291	-264713.698	-264739.829
F4	Gas	-358983.378	-358982.786	-359010.305
	COSMO	-358992.386	-358991.793	-359019.215

CONCLUSIONS

In the study, degradation mechanisms were estimated for three molecules and their reasons were explained by examining their energy values and electronegative atoms in the molecule, bond lengths and angles. In this study, possible reaction pathways were determined in the reaction between Covid agents and OH radical. The decomposition reaction requires energy. OH radicals are used to degrade Covid active ingredients. The lowest energy molecule has the most stable structure. Accordingly, we listed the Covid active ingredients from the most stable to the most unstable: Hesperidin -1365293.170 kcal/mol, Delta Viniferin -960021.090

kcal/mol, Afzelin -954891.660 kcal/mol. Our aim was to break down the Covid active ingredients down to the smallest harmless substances. As can be seen from the results, this fragmentation occurred theoretically. These results will guide experimental workers and determine the fragmentation mechanism.

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