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Removal of penicillin group antibiotics azlocillin, cloxacillin, methicillin from wastewater by DFT method

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Antibiotics administered to living things are excreted either unchanged or with little transformation in living metabolism. Discarded antibiotic residues should not be treated in conventional wastewater treatment plants and may enter the receiver directly. Low temperatures of antibiotic residues in the recipient environment may cause increased resistance of microorganisms, while high amounts may cause them to remain toxic. For this reason, wastewater containing antibiotic residues must be treated. Possible reactions of the penicillin group antibiotics were investigated using the DFT method, which is a molecular modeling method. The penicillin group antibiotic molecules examined are azlocillin, cloxacillin and methicillin. No previous studies have been conducted on the molecules examined. The optimized geometries were drawn with Gauss View 5.0 and then calculated with the Gaussian 09W program using functional density theory (DFT). The geometric structure (bond angles and bond lengths) and possible degradation products of all three molecules were calculated with the DFT method and the 6-31G(d) basis set. Thus, the possible degradation type of these three antibiotic molecules in water was determined. These results will guide experimental workers.

Keywords: Antibiotics, azlocillin, cloxacillin, methicillin, Gaussian 09, DFT

INTRODUCTION

Antibiotics are an important group within the antibacterial group. Antibiotics are chemical substances synthesized from various microorganisms such as bacteria, fungi and actinomycetes and prevent the development of other microorganisms or kill them. Today, some of the antibiotics are fully synthesized or the desired derivatives are prepared by semi-synthesis. That's why they are included in the chemotherapeutic class.

An ideal antibiotic should have a broad spectrum of microorganisms. It should have a bactericidal effect and not a bacteriostatic effect. Resistance should not occur easily. The potency should not change in long- and short-term use. It should not cause serious side effects. It should not cause sensitization in the organism. All methods should be used with the same effectiveness. It should dissolve well in water and should not decompose for a long time at room temperature. Absorption, distribution, metabolism and excretion properties must provide a rapid and continuous bactericidal effect. It should be easily accessible and cheap [1]. All bacteria have three growth phases: slow growth, rapid growth and rest periods. Antibiotics are effective during the fast and slow growth periods of bacteria. This interaction either kills bacteria or stops their development and reproduction.

Penicillins, aminoglycosides, cephalosporins, vancomycin, fluoroquinolones and bacitracin have bactericidal effects, while tetracyclines, macrolides and sulfonamides have bacteriostatic effects [2]. The presence of antibiotics in the aquatic environment is the subject of many studies in some countries. More than 30 antibiotic substances have been detected in sewage inlet and outlet water samples, surface waters, and even groundwater and drinking water. Metabolites or degradation products of antibiotics reach the aquatic environment through the application of sludge or manure to agriculturally used areas, or directly through animal feces on the land, through superficial rains, or by percolation in the deep layers of the earth. In this way, soils can act as a source of antibiotic pollution of the aquatic environment.

Owing to non-compliance with the necessary sanitary rules in fish farms, diseases occur frequently and cause great economic losses. The most common method of treating bacterial diseases of fish is the use of antibiotics and some other chemicals. The unconsumed portion of the antibiotics given to the fish by mixing them with the feed dissolves in water or settles on the ground. Some of the drug, which enters the environment with waste feed, is taken up by fish and crustaceans in the natural environment and accumulates in the body, reaching high concentrations.

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Overuse of antibiotics also encourages the development of pathogens that are resistant to standard antimicrobial practices. The antibiotics used have negative effects on other living things through the food chain or the aquatic ecosystem [3-7].

In this study, firstly, the initial geometries of the molecules were determined and geometric blocks based on DFT/B3LYP/6-31G(d) (B3LYP) were created. The energy values calculated from the DFT method include possible fragmentation reactions for each molecule. All programming was done by modeling the solvent effect in both the gas phase and the water phase.

METHODOLOGY

The reaction model used in this study is the reaction between azlocillin, cloxacillin, methicillin molecules and photo-generated •OH radicals [8]. Molecular models consist of average bond distances, geometric allowances of benzene rings, tetrahedral angles for sp3 hybridized carbon and oxygen atoms, and 120° for sp^2 hybridized carbon atoms. In the structure of hydroxylated radicals, the aromatic ring was produced planely outside the attack position. Due to the attack of the •OH radical on the carbon atom, the hybridization block was formed from sp^2 to sp^3 and assuming a tetrahedral angle with the C-H bond. Hydroxyl radicals forming organic compounds through single electron exchange by detachment of oxygen from single bonds, incorporation into double bonds, and loss of water from multiple hydroxyl radical additives. may change with systems. It is well known that serious problems arise in quantum calculations of open-shell molecules. Electronic developments, the absence of which is the main case of HF methods, are taken into account in DFT methods. The latter involve less spin contamination than HF methods, and these features include systems with effects suitable for programming. For this reason, the geometric structures of the reactants were made by the DFT method. The DFT method is a Gaussian 09 software program *via* B3LYP [9]. Frequencies were calculated to determine them as real minima on potential energy surfaces [10-12].

RESULTS AND DISCUSSION

In search of a reasonable mechanism for the photocatalytic degradation of azlocillin, cloxacillin, methicillin molecules, calculations were made with the DFT method to gain information about the region most sensitive to hydroxyl radical attacks. Figure 1 shows the optimized structures of azlocillin, cloxacillin, methicillin molecules.

The reaction paths of the three molecules shown in Figures 2-4 reveal that the specific regions of azlocillin, cloxacillin, methicillin molecules are close to those of the •OH radical. The predicted reaction pathways were validated by comparison with examples on simple structures from the literature, as described below. The lowest energy structure is a stable structure. The calculations in this disintegration were theoretically calculated and supported by looking at the Gibbs free energy values in Tables 1-3. Energy, enthalpy, Gibbs free energies of compounds are shown in Tables 1-3.

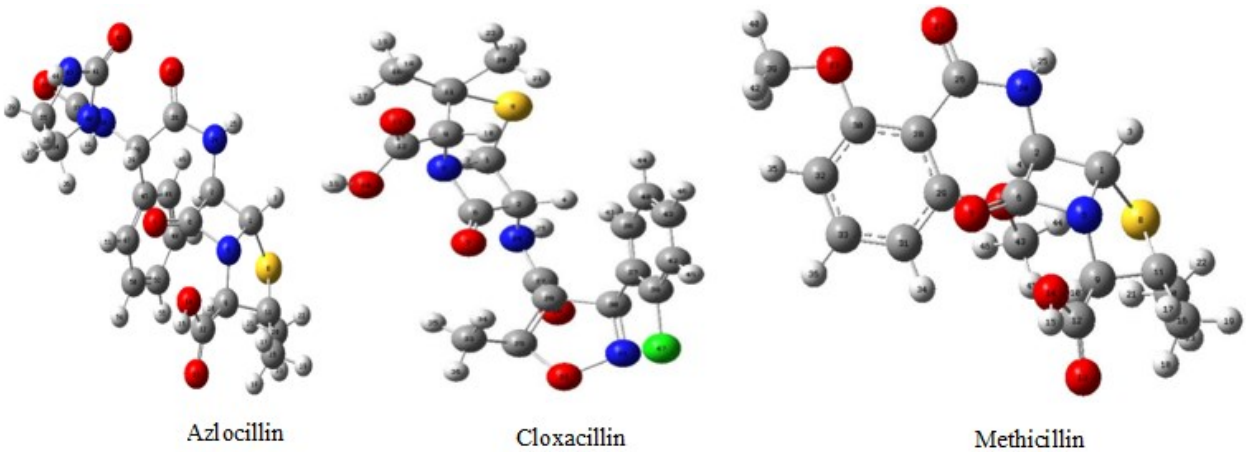

Fig. 1. Optimized geometric structure of azlocillin, cloxacillin, methicillin molecules by DFT method (grey, C; white, H; red, O; blue, N; green, Cl; yellow, S)

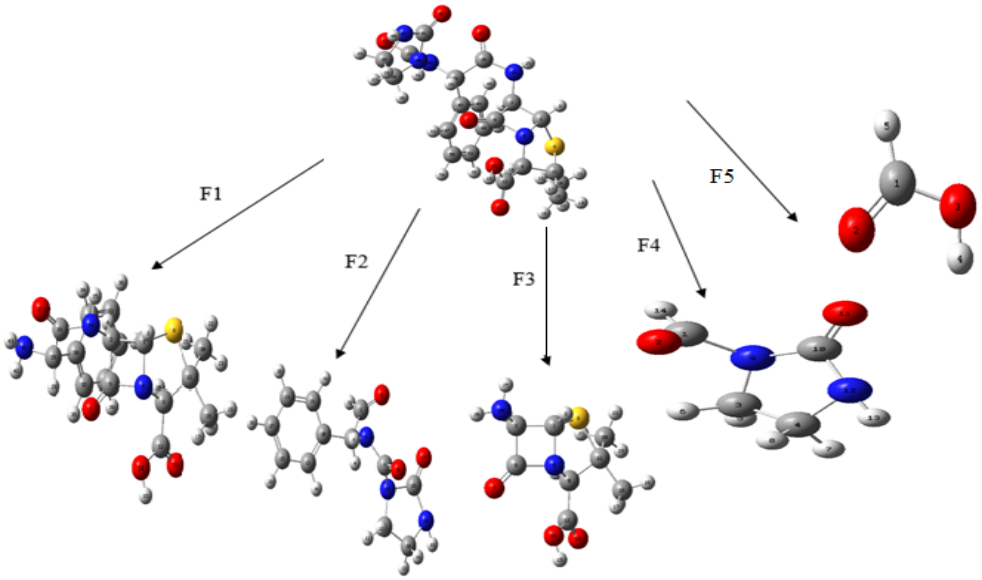

Fig. 2. Possible reaction pathways for the photocatalytic degradation of azlocillin (grey, C; white, H; red, O; blue, N; yellow, S)

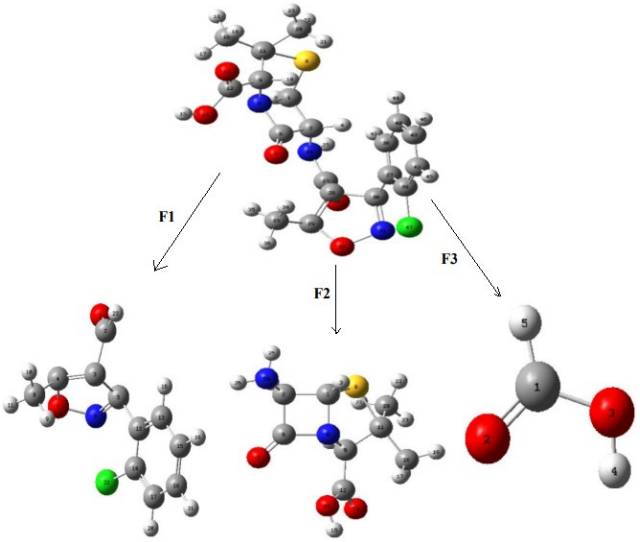

Fig. 3. Possible reaction pathways for the photocatalytic degradation of cloxacillin (grey, C; white, H; red, O; blue, N; green, Cl; yellow, S)

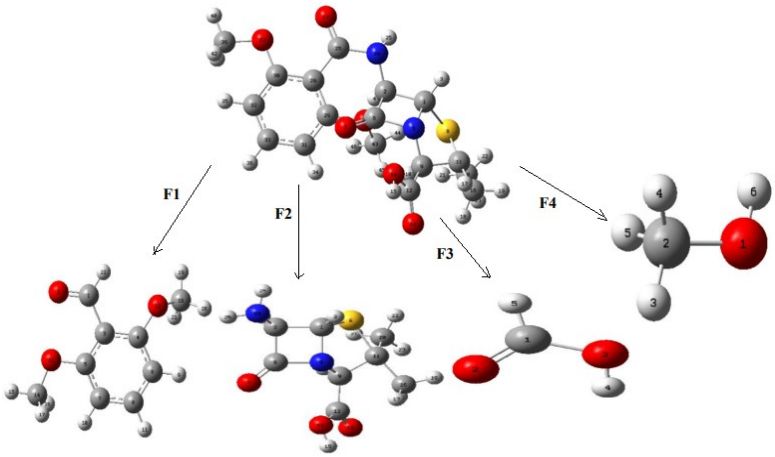

Fig. 4. Possible reaction pathways for the photocatalytic degradation of methicillin (grey, C; white, H; red, O; blue, N; yellow, S)

Table 1. Energy, enthalpy and Gibbs free energy values according to the DFT method.

Molecules	Phase	ΔE Energy (kcal mol^{-1})	ΔH Enthalpy (kcal mol^{-1})	ΔG Gibbs free energy (kcal mol^{-1})
Azlocillin	Gas	-1191540.257	-1191539.665	-1191599.153
	COSMO	*-1191556.146*	*-1191555.554*	*-1191615.422*
F1	Gas	-931289.848	-931289.256	-931339.481
	COSMO	*-931304.967*	*-931304.374*	*-931353.967*
F2	Gas	-536388.182	-536387.590	-536426.732
	COSMO	*-536395.613*	*-536395.021*	*-536435.109*
F3	Gas	-655872.8002	-655872.208	-655907.600
	COSMO	*-655882.548*	*-655881.956*	*-655917.185*
F4	Gas	-260979.003	-260978.410	-261003.316
	COSMO	*-260987.491*	*-260986.899*	*-261011.936*
F5	Gas	-119049.984	-119049.392	-119067.076
	COSMO	*-119054.194*	*-119053.602*	*-119071.294*

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

Molecules	Phase	ΔE Energy (kcal mol^{-1})	ΔH Enthalpy (kcal mol^{-1})	ΔG Gibbs free energy (kcal mol^{-1})
Cloxacillin	Gas	-1338943.463	-1338942.871	-1338999.588
	COSMO	*-1338958.286*	*-1338957.694*	*-1339014.568*
F1	Gas	-683798.496	-683797.904	-683833.100
	COSMO	*-683804.928*	*-683804.335*	*-683839.470*
F2	Gas	-655872.800	-655872.208	-655907.600
	COSMO	*-655882.548*	*-655881.956*	*-655917.185*
F3	Gas	-119049.984	-119049.392	-119067.076
	COSMO	*-119054.194*	*-119053.602*	*-119071.294*

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

Molecules	Phase	ΔE Energy (kcal mol^{-1})	ΔH Enthalpy (kcal mol^{-1})	ΔG Gibbs free energy (kcal mol^{-1})
Methicillin	Gas	-1291030.538	-1291029.945	-1291096.658
	COSMO	*-1291051.841*	*-1291051.249*	*-1291118.715*
F1	Gas	-360463.595	-360463.003	-360494.578
	COSMO	*-360472.131*	*-360471.539*	*-360503.087*
F2	Gas	-655872.800	-655872.208	-655907.600
	COSMO	*-655882.548*	*-655881.956*	*-655917.185*
F3	Gas	-119049.984	-119049.392	-119067.076
	COSMO	*-119054.194*	*-119053.602*	*-119071.294*
F4	Gas	-72577.466	-72576.873	-72593.789
	COSMO	*-72580.673*	*-72580.081*	*-72597.018*

CONCLUSIONS

In this study, fragmentation mechanisms for three molecules were determined. The energy values, electronegative atoms in the molecule, bond lengths and the angles are examined and explained. In the study, antibiotic active ingredients and water molecules were examined. Possible reaction pathways were determined for the reaction between the fission reaction producing the energy it requires. That's why these chemicals break down the OH in water. using radicals. The most stable structure of a molecule is its lowest energy state. When we rank the antibiotic active ingredients from the most stable to the most unstable, the order is: cloxacillin -1338943.463 kcal/mol, methicillin -1291030.538 kcal/mol, azlocillin -1191540.257 It is in the form of kcal/mol. Our aim is to reduce the antibiotic active ingredients to the smallest harmless ones. It was to

break it down to substances. As a result, the first molecule, azlocillin, when we rank the 5 fragments, which are the breakdown products, from the most stable to the unstable, F1 is -931289.848 kcal/mol, F3 -655872.800 kcal/mol, F2 -5363881.828 kcal/mol, F4 -260979.003 kcal/mol, F5 is -119049.984 kcal/mol. Disintegration of the second molecule, cloxacillin when we rank the 3 fragments from the most stable to unstable, F1 is -683798.496 kcal/mol, F2 it is -655872.800 kcal/mol, F3 is -119049.984 kcal/mol. Methicillin, the 3rd molecule when we rank the 4 fragments, which are the breakdown products of the molecule, from the most stable to the unstable, F2 -655872.800 kcal/mol, F1 -360463.595 kcal/mol, F3 -119049.984 kcal/mol, F4 -72577.466. As can be seen from the results, this fragmentation was realised. These results determine the mechanism and will guide experimental workers. Prediction of the degradation of molecules occurred through cleavages of intramolecular fragments, followed by •OH radical reactions. With this reaction, the fragments turn into smaller species such as CO_2, NO_3^- and NH_4^+.

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