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Modeling of Anthocyanin Derivatives as Anti-UV Agents

Khusna Arif Rakhman*[1, 2], Khadijah[1], Muhammad Ikhlas Abdjan[1], Nurbaiti Kumendong[2], and Setyani Dian Puspitasari[2]

1. Department of Chemistry Education, Khairun University, Ternate 97751, Indonesia
2. Environmental Laboratory, Khairun University, Ternate 97751, Indonesia

Abstract: The optimization of molecular geometry and the modeling of electronic transition to anti-UV activities on anthocyanin derivatives in computationally have been conducted using the Hyperchem 8.0.10 application. Semi-empirical PM3 method is applied and the parameter of data is measured *i.e.* charge and total energy. The objective of study is to get a potential model of anthocyanin derivatives as anti-UV agents. The results show that each anthocyanin derivative has optimal geometry in stable energy. Electronic transition modeling of anthocyanin derivatives has been done using semi-empirical ZINDO/s method with a limited change of gradient 0.01 kcal/(Å.mol). The results show that the transition type in 10 anthocyanin derivatives is $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ with anti UV activity in the UV-A and UV-C wavelength regions. Electron excitation for each anthocyanin derivative occurs in four molecule orbitals. The energy difference of HOMO-LUMO shows that malvidin compound has the smallest energy gap which around 5.61, whereas the luteolinidin compound has the biggest energy gap which around 5.94 eV.

Keywords: Anthocyanin derivatives, anti-UV activity, ZINDO/s.

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***Corresponding author. E-mail:** khusna.arif.rakhman@gmail.com.

INTRODUCTION

UV electromagnetic wave radiation is divided into three parts based on its wavelength range, namely UV-C (100-280 nm), UV-B (280-320 nm) and UV-A (320-400 nm) (1). Chemical compounds that have the ability to interact with UV electromagnetic waves are compounds that have chromophore and auxochrome groups because of their ability to absorb at certain wavelengths (2). The combination of several aromatic compounds such as cinnamic acid derivatives, benzophenone, aminobenzoate, and anthocyanins have the potential as UV absorbing agents because of the content of chromophore and auxochrome groups in these compounds (3, 4).

The UV interactions with chemical compounds can be studied by computational modeling, instead of experimental measurements. Modeling of UV interaction with chemical compounds that lead to the potential of chemical compounds in counteracting UV (anti-UV activity) can be known through the relationship of intensity with absorbed wavelengths (5). Modeling of UV activity on the chemical compound can be determined by electronic transition modeling using semi-empirical methods (6, 7). The ZINDO/s method (Zerner's Intermediate Negative of Differential

Overlap/Spectroscopy) is one of the semi-empirical methods that is led to model electronic transitions in the form of discontinuous spectra (8, 9). Compounds that have the potential as anti-UV agents will show peaks with high-intensity values in ZINDO/s modeling (10).

Anthocyanin (Figure 1) is one of the secondary metabolites of the flavonoid family which is usually contained in fruits and vegetables that are red or purple such as *Aerva sanguinolenta*, and *Hylocereus undatus* (11). Research on anthocyanin used as natural dyes, antioxidants and anti-UV agents (12, 13, 14). Unlike other flavonoid derivatives, anthocyanin have attractive color characteristics to investigate their activity against UV radiation. This study aims to get a potential model of anthocyanin derivatives as anti-UV agents. The modeling object of this study was several derivatives of anthocyanins like Aurantinidin, Cyanidin, Delphinidin, Europinidin, Malvidin, Pelargonidin, Peonidin, Petunidin, and Rosinidin. The basic structure of anthocyanidin has seven functional groups which will be combined with substitution with -H, -OH and $-OCH_3$ substituents. This article reports the potential of anthocyanin as anti-UV agents in the form of electronic transition modeling. Electron transition characteristics that occur in anthocyanin derivatives will reflect the energy needed when subjected to light at certain wavelengths (15, 16). Then, the determination of the ease of derivation of anthocyanin that experience electron excitation from HOMO to LUMO is the easiest to see photosensitivity properties which will affect their potential as anti UV agents (17). The modeling results of anthocyanin derivative compounds can be used to conduct further research that leads to the development of dyes for food, medicine, and materials, especially for UV capture materials such as solar cells.

METHODOLOGY

Geometry Optimization of PM3 Anthocyanin

The modeling of molecule geometry optimization and molecule energy calculations are using semi-empirical PM3 method (18), in limited change of gradient around 0.01 kcal/(Å.mol) till reach nearly limited gradient based on the Polak-Ribiere method. The purpose of molecular geometry optimization is to obtain a stable molecule geometry (19).

Electronic Transition Modeling Analysis and Anthocyanin UV Spectra

The modeling on structure results in semi empirical PM3 geometry optimization is continued to measure the single point of configuration interaction (CI) by using semi empirical ZINDO/s methods. This method is used to get spectra electronic transition data. Modeling of orbital molecule on single excitation (CI) uses two levels on HOMO-LUMO energy.

RESULTS AND DISCUSSION

Geometry Optimization of Anthocyanin-Derived Compounds

Optimization of molecular geometry of anthocyanin-derived compounds using PM3 semi-empirical method shows data in the form of molecular structure and charge accompanied by energy, to be able to determine the stability of the molecular geometry. Table 1 shows the existence of 7 different functional groups in the 10 molecules of anthocyanin derivatives from the basic structure of the compounds which have 3 benzene rings with simple conjugated bonds. The functional group substitution produces 10 anthocyanin derivatives with a combination of substitute groups in the form of -H, -OH and $-OCH_3$.

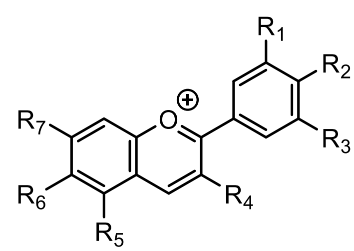


Figure 1. The molecular structure of anthocyanins.

Table 1: Derivatives of Anthocyanin

Derivatives of Anthocyanin	R_1	R_2	R_3	R_4	R_5	R_6	R_7
Aurantinidin	-H	-OH	-H	-OH	-OH	-OH	-OH
Cyanidin	-OH	-OH	-H	-OH	-OH	-H	-OH
Delphinidin	-OH	-OH	-OH	-OH	-OH	-H	-OH
Europinidin	-OCH_3	-OH	-OH	-OH	-OCH_3	-H	-OH
Luteolinidin	-OH	-OH	-H	-H	-OH	-H	-OH
Malvidin	-OCH_3	-OH	-OCH_3	-OH	-OH	-H	-OH
Pelargonidin	-H	-OH	-H	-OH	-OH	-H	-OH
Peonidin	-OCH_3	-OH	-H	-OH	-OH	-H	-OH
Petudinin	-OH	-OH	-OCH_3	-OH	-OH	-H	-OH
Rosinidin	-OCH_3	-OH	-H	-OH	-OH	-H	-OCH_3

Table 2: Geometry Optimization of Anthocyanin

Derivatives of Anthocyanin	Total Energy (kcal/mol)	Binding Energy (kcal/mol)	Heat Formation (kcal/mol)
Aurantinidin	-85338.1028542	-3510.6412492	-16.8152492
Cyanidin	-85339.2443358	-3511.7827308	-17.9567308
Delphinidin	-92116.2174990	-3616.2400320	-62.8550320
Europinidin	-98986.3988524	-4150.3655134	-46.7925134
Luteolinidin	-78572.3759095	-3417.4301665	16.8368335
Malvidin	-98986.0858247	-4150.0524857	-46.4794857
Pelargonidin	-78567.4389408	-3412.4931978	21.7738022
Peonidin	-88775.4466615	-3779.9571205	-11.0371205
Petudinin	-95552.6605097	-3884.6551067	-56.1761067
Rosinidin	-92212.3418400	-4048.8243630	-4.8103630

The results of molecular geometry optimization on 10 anthocyanin derivatives using semi-empirical method PM3 showed that pelargonidin are compounds that have the smallest total energy (Table 2). The bond energy and heat of formation are one part of the total energy of the molecule derived from anthocyanin. The lowest or near zero total energy and formation heat obtained from geometry optimization shows the stability of a molecule (20).

Electronic Transitions and UV Spectra of Anthocyanin Derivative Compounds

Electronic transition modeling was performed using semi-empirical ZINDO/s method with data parameters taken in the form of wavelength, intensity, MO level, and HOMO-LUMO energy to study anti-UV activity of anthocyanin derivatives. Wavelengths and intensity values read on each anthocyanin derivative compound contained 4 peaks with a range of values of wavelengths of 200-400 nm in the UV region (Table 3). Discontinuous spectrum modeling on these 10 compounds has an orbital molecular level which is useful for studying the ease of electron excitation through the energy gap approach in the valence band (24).

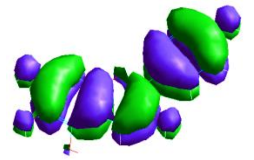
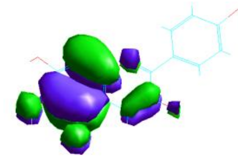
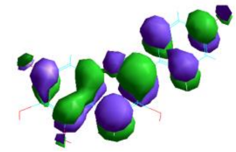
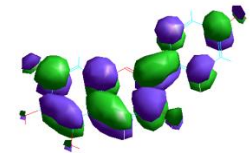
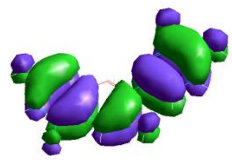
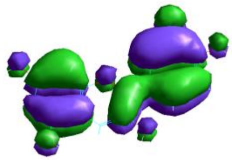
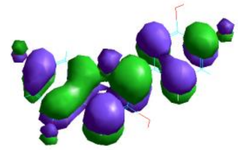
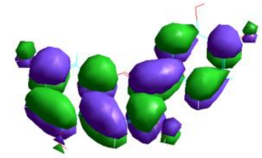
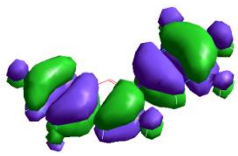
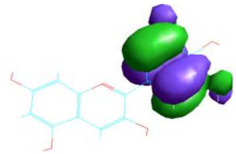
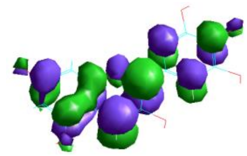
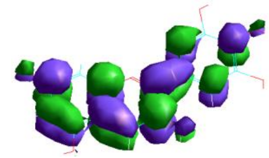
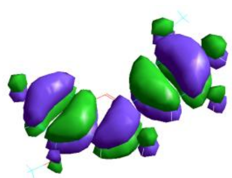
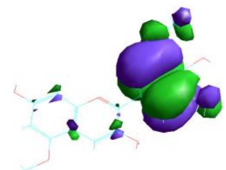
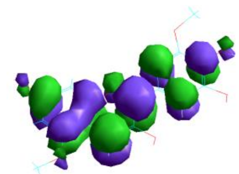
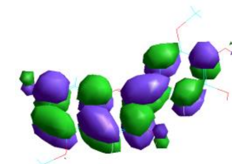
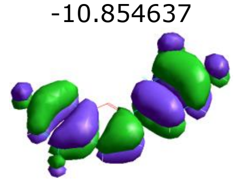
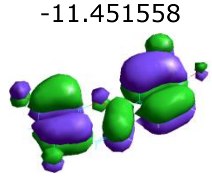
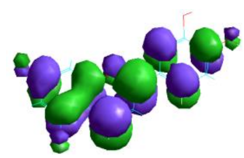
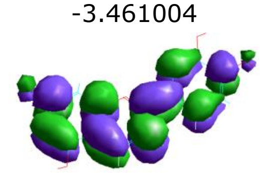
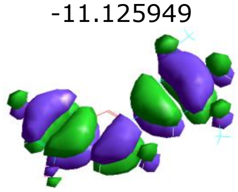
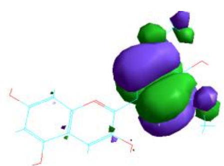
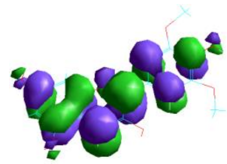
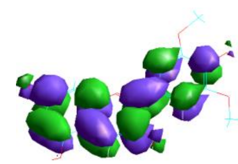
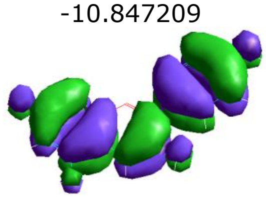
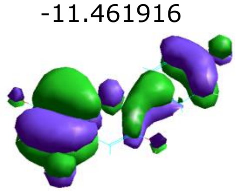
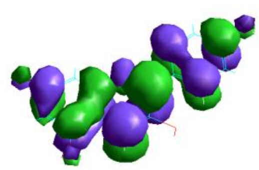
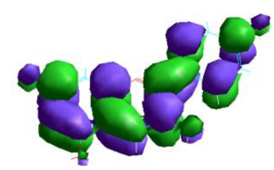
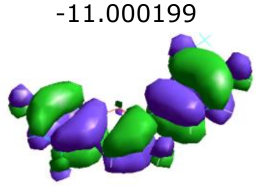
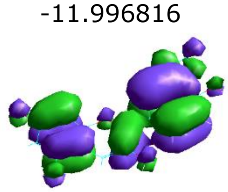
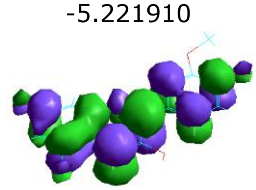
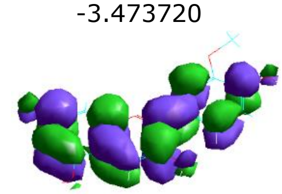
Determination of the transition type in 10 anthocyanin derivatives for each wavelength shows the transition types n to π^* and π to π^* at the 4 transition peaks. Transition n to π^* occurs because there is a simple conjugated chromophore group in aromatic rings and the transition π to π^* shows the substitution group (R1-R7) which is an auxochrome group which influences the wavelength shift. The intensity value read on the electronic transition causes a wavelength shift to occur. Transitions that occur at these wavelengths indicate the potential for anti-UV activity in the UV-A and UV-C regions for 10 anthocyanin derivatives.

Table 3 : Electronic Transition and UV Activity of Derivative of Anthocyanin

Derivatives of Anthocyanin	λ(nm)	Osc	MO Level	Transition level	UV Activity
Aurantinidin	456.3	1.0958	53→54	n→π*	UV-A - UV-C
	386.1	0.0741	52→54	n→π*	
	268.4	0.4613	53→55	n→π*	
	249.5	0.4097	52→55	π→π*	
Cyanidin	459.0	1.1685	53→54	n→π*	UV-A - UV-C
	360.1	0.0207	52→54	n→π*	
	267.0	0.3221	53→55	n→π*	
	232.9	0.2948	52→55	π→π*	
Delphinidin	449.3	1.1335	56→57	n→π*	UV-A - UV-C
	383.2	0.0492	55→57	n→π*	
	265.7	0.2854	56→58	n→π*	
	232.6	0.1081	55→58	π→π*	
Europinidin	450.2	1.1245	62→63	n→π*	UV-A - UV-C
	386.6	0.0465	61→63	n→π*	
	266.1	0.2908	62→64	n→π*	
	234.5	0.1185	61→64	π→π*	
Luteolinidin	425.4	1.1514	50→51	n→π*	UV-A - UV-C
	340.7	0.0152	49→51	n→π*	
	255.5	0.2273	50→52	n→π*	
	227.2	0.3056	49→52	π→π*	
Malvidin	451.3	1.1402	62→63	n→π*	UV-A - UV-C
	389.8	0.0452	61→63	n→π*	
	266.8	0.2773	62→64	n→π*	
	234.2	0.1085	61→64	π→π*	
Pelargonidin	452.1	1.1973	50→51	n→π*	UV-A - UV-C
	346.0	0.0220	49→51	n→π*	
	265.0	0.3706	50→52	n→π*	
	238.6	0.4060	49→52	π→π*	
Peonidin	453.8	1.1663	56→57	n→π*	UV-A - UV-C
	361.3	0.0143	55→57	n→π*	
	266.6	0.3174	56→58	n→π*	
	230.0	0.2732	55→58	π→π*	
Petudinin	450.7	1.1407	59→60	n→π*	UV-A - UV-C
	384.1	0.0481	58→60	n→π*	
	266.7	0.2772	59→61	n→π*	
	232.5	0.0973	58→61	π→π*	
Rosinidin	454.1	1.1578	59→60	n→π*	UV-A - UV-C
	359.6	0.0123	58→60	n→π*	
	266.6	0.3289	59→61	n→π*	
	229.9	0.2772	58→61	π→π*	

One of the parameters measured in determining the UV activity of anthocyanin derivatives is HOMO (eV) and LUMO (eV) energy. The Highest Occupied Molecular Orbitals (HOMO) are the highest energy molecular orbitals filled with electrons and the Lowest Unoccupied Molecular Orbitals (LUMO) are the lowest energy molecular orbitals that are not filled with electrons (25). The energy gap between HOMO and LUMO is known as the energy gap (gEg), where the gap energy is the minimum energy needed to excite electrons from HOMO to LUMO (26). The energy gap (eV) between HOMO-LUMO will reflect the ease of an excited electron when subjected to an electromagnetic wave with a certain wavelength.

Table 4. HOMO-LUMO Energy Level of Anthocyanin Derivatives.

Derivatives of Anthocyanin	HOMO (eV)	HOMO-1 (eV)	LUMO (eV)	LUMO+1 (eV)
Aurantinidin	 -11.035057	 -11.698295	 -5.318554	 -3.559058
Cyanidin	 -11.009844	 -11.780312	 -5.322355	 -3.550417
Delphinidin	 -10.965636	 -11.606985	 -5.318181	 -3.557562
Europinidin	 -10.854637	 -11.451558	 -5.216126	 -3.461004
Luteolinidin	 -11.125949	 -11.870198	 -5.185068	 -3.507093
Malvidin	 -10.847209	 -11.461916	 -5.235400	 -3.476526
Pelargonidin	 -11.000199	 -11.996816	 -5.221910	 -3.473720
Peonidin	 -10.916036	 -11.651897	 -5.217128	 -3.463220

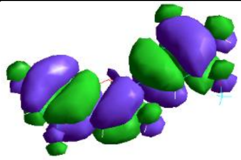
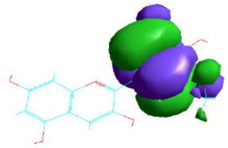
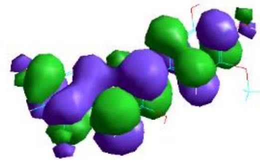
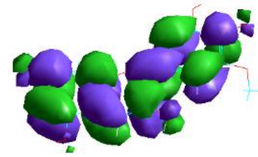
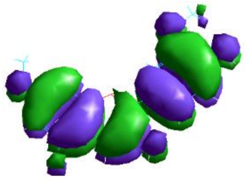
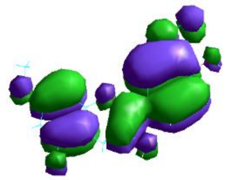
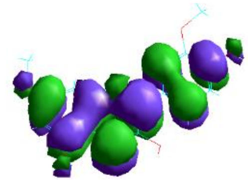
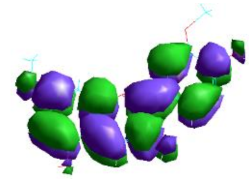
Petudinin	 -10.903310	 -11.565510	 -5.278661	 -3.519875
Rosinidin	 -10.875191	 -11.615891	 -5.173106	 -3.418870

Table 5: HOMO-LUMO Energy Difference

Derivative of Anthocyanin	E_{LUMO}-E_{HOMO} (eV)	E_{LUMO}-E_{HOMO-1} (eV)	E_{LUMO+1}-E_{HOMO} (eV)	E_{LUMO+1}-E_{HOMO-1} (eV)
Aurantinidin	5.71	6.37	7.47	8.13
Cynidin	5.68	6.45	7.45	8.22
Delphinidin	5.64	6.24	7.39	8.04
Europinidin	5.63	6.23	7.39	8.00
Luteolinidin	5.94	6.68	7.61	8.36
Malvidin	5.61	6.22	7.37	7.98
Pelargonidin	5.77	6.77	7.52	8.52
Peonidin	5.70	6.43	7.45	8.18
Petudinin	5.62	6.28	7.38	8.04
Rosinidin	5.70	6.44	7.45	8.19

Modeling of HOMO energy and LUMO anthocyanin derivatives were carried out using the semi-empirical method of ZINDO/s. The modeling results of changes in energy resulting from UV interactions with compounds indicate that there are four molecular orbitals that experience electron transitions (Table 4), namely HOMO (0 and -1) and LUMO (0 and +1) for every 10 anthocyanin derivatives. The interaction between anthocyanin and UV wave compounds in this modeling is indicated by the electron transition from HOMO to LUMO for each molecular orbitals of anthocyanin compounds derived from HOMO to LUMO, HOMO-1 to LUMO, HOMO to LUMO + 1 and HOMO-1 to LUMO +1. The lowest HOMO-LUMO Energy Difference based on modeling using semi-empirical ZINDO/s method is found in malvidin compound with a value of 5.61 eV (Table 5).

CONCLUSION

The molecular geometry optimization of anthocyanin derivatives was carried out using the semi-empirical method of PM3 which showed a stable change in charge and energy with the lowest total energy value in the pelargonidin of -78567 (kcal/mol). Determination of electronic transitions on each anthocyanin derivative compound shows that there are four electron transition peaks with transition types, namely n to π^* and π to π^*. The potential of anthocyanin derivatives as anti UV agents shows activity in the UV-A and UV-C wavelength regions. Malvidin compounds have a better potential than some anthocyanin derivatives as anti UV based on a review of the HOMO-LUMO energy difference of 5.61 eV.

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