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Computational Bioinformatics Study of Noni to Lower Cholesterol Levels (Morinda citrifolia)

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ABSTRACT

Increased cholesterol levels or also known as hypercholesterolemia is one of the risk factors for coronary heart disease. A person can be categorized as having hypercholesterolemia if the cholesterol level is declared high if in adults the cholesterol value reaches> 240 mg/dl while in children and adolescents the total cholesterol value reaches 200 mg/dl or more has been declared high. To reduce hypercholeterolemia or cholesterol levels in the blood, it can be done using traditional medicine, one of which is noni fruit. Noni fruit (Morinda citrifolia) can reduce total blood cholesterol, LDL, triglycerides and increase HDL and can improve the histology structure of the aortic vessels (thickening of the tunica media) in mice given a high-fat diet.

Keywords : Cholesterol or Hypercholesterolemia, Noni

1. INTRODUCTION

Increased cholesterol levels or also known as hypercholesterolemia is one of the risk factors for coronary heart disease [1][2][21]. In Indonesia alone, there are about 36 million people or about 18% of the Indonesian population who suffer from this blood lipid disorder [3][4]. Of that number, 80% of patients died suddenly from a heart attack and 50% of them were asymptomatic [5]. Hypercholesterolemia is defined as an increase in plasma cholesterol levels above normal [6][7]. Cholesterol levels in adults are declared high if they reach a value of >240 mg/dl while in children and adolescents the total cholesterol value reaches 200 mg/dl or more has been declared high [8][9][10].

Actually cholesterol in appropriate levels is actually needed by the body in helping to build new cells so that the body can continue to function normally [11][12]. Cholesterol serves to help the body produce vitamin D, a number of hormones, and bile acids to digest fat[13][14]. In the blood, cholesterol is carried by proteins [15]. The combination of the two is called a lipoprotein. The two main types of lipoproteins are low-density lipoprotein (LDL) commonly referred to as bad cholesterol and high-density lipoprotein (HDL) commonly referred to as good cholesterol [16][17].

The duty of LDL is to transport cholesterol from the liver to the cells that need it [18]. However, if the amount of cholesterol exceeds the need, it can settle on the walls of the arteries causing disease[19][22]. Meanwhile, HDL is responsible for transporting cholesterol back into the liver as opposed to LDL. In the liver, cholesterol will be destroyed or excreted by the body through feces or feces [20][23].

To reduce hypercholeterolemia or cholesterol levels in the blood, it can be done using traditional medicine, one of which is noni fruit [24][25]. Noni fruit (Morinda citrifolia) can reduce total blood cholesterol, LDL, triglycerides and increase HDL and can improve the histological structure of the aortic vessels (thickening of the tunica media) of mice given a high-fat diet [26][27].

2. LITERATURE REVIEW

Noni (Morinda citrifolia L.) is a plant that has long been used by the community as a food ingredient as well as treatment. Noni contains scopoletin which functions to dilate narrowed blood vessels, so that the heart is not too hard to pump blood and blood pressure becomes normal. The discovery of medicinal plants that have potential as hypertension can now use the Molecular docking method [28]. Molecular docking can help in silico screening to predict whether the chemical content of the active ingredients in certain plants has the potential as antihypertensive by comparing it with a compound with known antihypertensive effect [29].

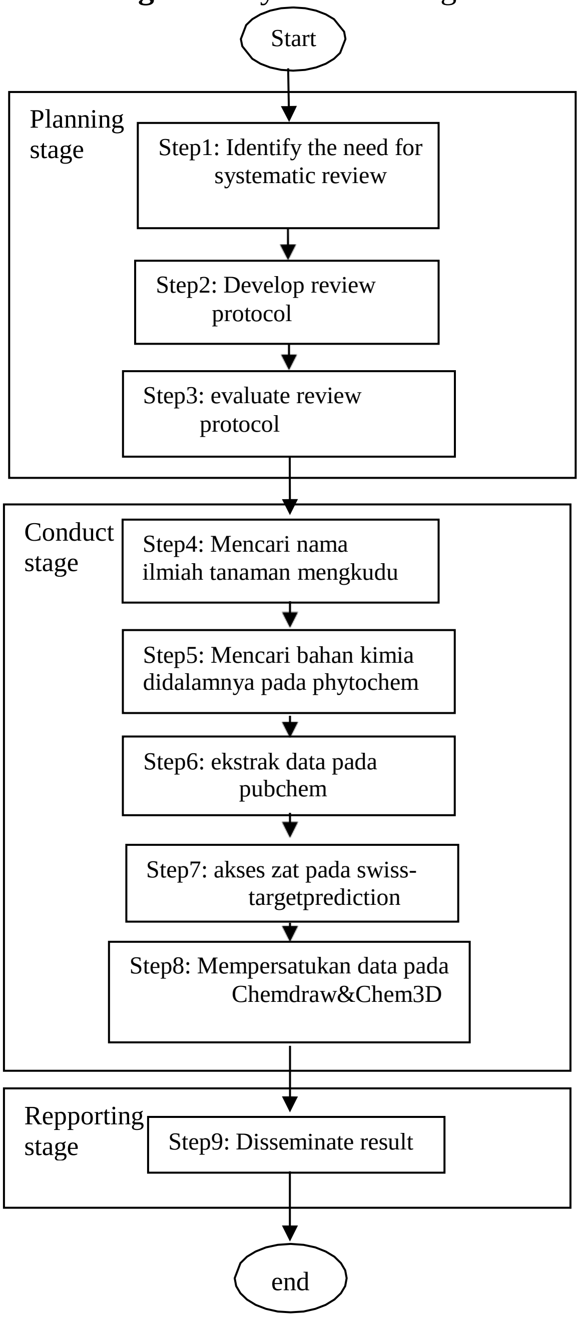
According to the results of the study, giving noni (Morinda citrifolia) capsules consisting of 90% dry extract of noni fruit and 10% filler can reduce total blood cholesterol levels. Noni (Morinda citrifolia) is also known as noni fruit. Noni is green and has black spots, and has a bitter taste. Noni is a fruit that is commonly found in Australia, India, and Southeast Asia, including in Indonesia [30].

3. EXPERIMENTAL

This research is a bioinformatics study with noni fruit samples to determine the active compounds in it by analyzing its structure and content through Phytochem https://phytochem.nal.usda.gov/, PubChem https://pubchem.ncbi.nlm.nih.gov/ , and Swiss target http://swisstargetprediction.ch/, as well as chemdraw and chem3d.

The chemical compounds found in the noni fruit, look at the content and active compounds used in phytochem, in phytochem we will use the active sentawa in the noni fruit, the active compounds that we got earlier we checked the structure, properties, and smile through pubchem, swiss target and chemdraw and chem3d aplikasi apps

Figure 1. Systematic Diagram



The implementation of this research aims to utilize regional plants as medicine to cure diseases. In addition, this study is an observational descriptive study conducted with an objective condition by looking back (retrospectively). The plants tested were noni fruit.

Furthermore, these plants were identified using Dr. Duke's Phytochemical and Ethnobotanical Database with the scientific name Morinda citrifolia. The search on the site aims to see the chemical compounds contained in these plants.

After that, one by one the chemical compounds were extracted in pubchem and the compound elements were taken in Isomeric SMILES then entered the compound elements in Swisstarget prediction to see which percentage of the compound contained a lot. The next step is to copy the IUPAC Name in Pubchem earlier, and access to Chemdraw and make optimizations with Chem3d to see a 3D structure image and how much energy is generated.

The last step is the disseminate result, which from the chemical obtained from swisstarget prediction, the result is an enzyme.

4. RESULTS AND DISCUSSION

4.1 Results

This research is viewed from the number of people who experience Diabetes Mellitus. Which is where most people do not have a healthy diet and think that DM is seen from heredity only. Whereas various factors that cause this disease are obesity, overeating, lack of exercise, and the most important supporting factor is an unhealthy lifestyle .

Based on the observations that have been made with many people living an unhealthy lifestyle and not regulating an unhealthy diet, this scientific paper was written. In order to make us more productive again in carrying out activities without experiencing disturbances, especially DM disease, where the complaint that often occurs is feeling tired quickly.

In overcoming the problem of DM among the community, the author urges to make lifestyle changes for the better. Which can be done by exercising 3-4 times a week and reducing food portions. The point here is not to reduce the food ration that should be 3 times a day to 2 times a day, but this is done by replacing carbohydrates from rice. Because we both know that rice is the food that contains the most glucose, which can cause obesity if we eat too much rice and can cause DM. To evaluate the occurrence of this problem, it is better if we replace the carbohydrates obtained from rice with purple sweet potatoes. By eating purple sweet potatoes, one of the substances contained in it is dipeptidyl peptidase which is an enzyme and binding protein found in various tissues including the liver, kidneys, pancreas , and endothelial cells that can function in maintaining blood sugar levels in the body.

Activities Count	Chemical	Plant Part	Low PPM	High PPM	StdDev
0	(Z)-6-DODECENO-GAMMA-LACTONE	Fruit		0.04	
0	(Z,Z)-2,5-UNDECADIEN-1-OL	Fruit		0.18	
0	1-BUTANOL	Fruit		0.03	
0	1-HEXANOL	Fruit		0.05	
0	2-HEPTANONE	Fruit		0.15	
0	2-METHYL-BUTANOIC-ACID	Fruit		0.23	
0	2-METHYL-HEXANOATE	Fruit		0.16	
0	2-METHYL-PROPANOIC-ACID	Fruit		0.05	

0	3-HYDROXY-2-BUTANONE	Fruit		0.03	
0	3-METHYL-2-BUTEN-1-OL	Fruit		0.13	
0	3-METHYL-3-BUTEN-1-OL	Fruit		1.78	
0	3-METHYL-THIOPROPANOIC-ACID	Fruit		0.18	
9	ASPERULOSIDE	Fruit		480	
44	SCOPOLETHIN	Fruit		0.85	-0.87314
87	ROUTINE	Fruit		500	-0.59649
20	BENZOIC-ACID	Fruit		8	-0.6617
9	BENZYL-ALCOHOL	Fruit		0.02	-0.69642
53	BETA-CAROTENE	Fruit		5.2	-0.14075
76	EUGENOL	Fruit		0.01	-0.70711
60	LIMONNE	Fruit		0.17	-0.75018
27	LINOLEIC-ACID	Fruit		0.02	-0.3554
6	MYRISTIC-ACID	Fruit		0.06	-0.26914
2	NONANOIC-ACID	Fruit		0.01	-0.74125
5	OCTANOIC-ACID	Fruit		25	1.714856
18	OLEIC-ACID	Fruit		0.03	-0.48074
13	PALMITIC-ACID	Fruit		0.21	-0.36553
4	PARAFFIN	Fruit			

Figure 2. The main chemical compounds found in noni

The following is data on chemical compounds in noni that have been analyzed using pubchem, chemdraw ultra, chemdraw 3D and swisstarget prediction.

1. (Z)-6-DODECENO-GAMMA-LACTONE

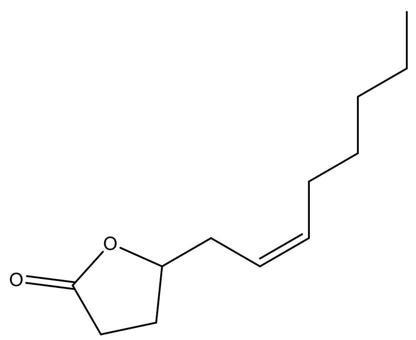


Figure 3. 5-[(Z)-oct-2-enyl]oxolan -2-one

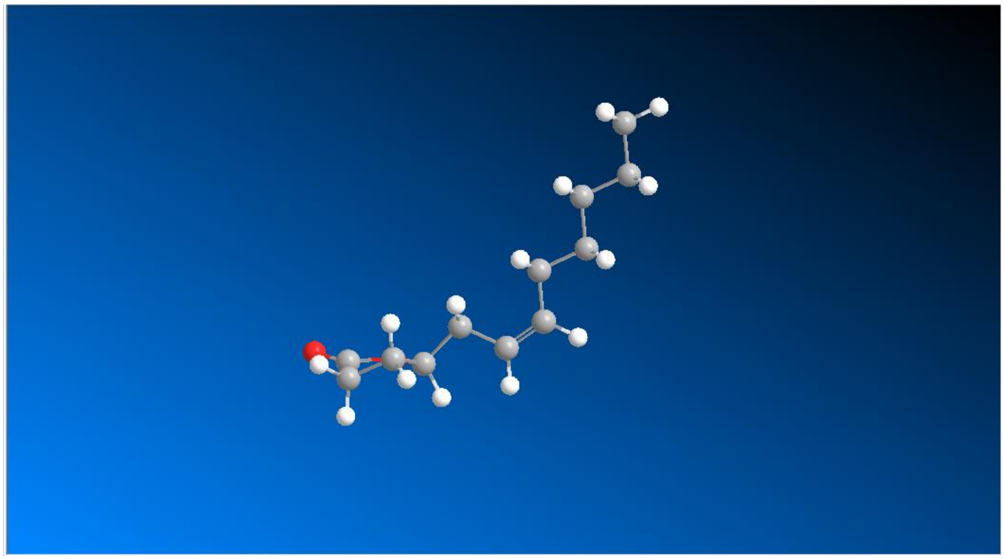


Figure 4. Prior Optimizing

Atom	X (Å)	Y (Å)	Z (Å)
O(1)	-31,969	-23.231	-12,820
C(2)	-45,640	-23.948	-0.8527
C(3)	-45.460	-28,817	4.028472
C(4)	-32,432	-23.157	10,839
C(5)	-23.516	-24.574	-0.1306
O(6)	-55.406	-21,197	-15,082
C(7)	-12.889	-13,665	-0.1306
C(8)	0.490278	-19932	-0.1306
C(9)	11,624	-12,216	-0.1306
C(10)	10.255	1.86875	-0.1306
C(11)	24,086	6.297222	-0.1306
C(12)	22,692	24,234	-0.1306
C(13)	36.523	30,610	-0.1306
C(14)	35,130	45,776	-0.1306
H(15)	-54.106	-24,800	11,546
H(16)	-46,253	-39,873	4.727083
H(17)	-28,520	-29.044	19,437
H(18)	-33,227	-12,729	14,646
H(19)	-18,290	-34,401	-0.1306
H(20)	-14,059	-0.7354	5.407639
H(21)	-14,060	-0.7347	-10,394
H(22)	1.189583	-30,886	-0.1306
H(23)	21,614	-16,821	-0.1306
H(24)	3.261111	4.097917	-10,398

Figure 5. Cartesian table

Atom	Bond Atom	Bond Length (Å)	Atomic Angle	Angle (°)	2nd Angle Atom	2nd Angle (°)	2nd Angle Type
C(2)							
O(1)	C(2)	14,347					
C(3)	C(2)	15.133	O(1)	1,067,467			
C(4)	C(3)	15,072	C(2)	1,018,831	O(1)	311,735	Dihedral
C(5)	O(1)	14,347	C(2)	1,084,529	C(3)	-121.087	Dihedral
C(7)	C(5)	15,230	O(1)	1,101,237	C(4)	1,101,237	Pro-R
O(6)	C(2)	12,080	O(1)	1,266,267	C(3)	1,266,267	Pro-R
C(8)	C(7)	14,970	C(5)	1,095,000	O(1)	-1,212,682	Dihedral
C(9)	C(8)	13370	C(7)	1,200,000	C(5)	-1,800,000	Dihedral
C(10)	C(9)	14,970	C(8)	1,200,000	C(7)	-0.0000	Dihedral
C(11)	C(10)	15,230	C(9)	1,095,000	C(8)	-1,800,000	Dihedral
C(12)	C(11)	15,230	C(10)	1,095,000	C(9)	-1,800,000	Dihedral
C(13)	C(12)	15,230	C(11)	1,095,000	C(10)	-1,800,000	Dihedral
C(14)	C(13)	15,230	C(12)	1,095,000	C(11)	-1,800,000	Dihedral
H(22)	C(8)	11,000	C(7)	1,200,000	C(9)	1,200,000	Pro-S
H(23)	C(9)	11,000	C(8)	1,200,000	C(10)	1,200,000	Pro-S
H(15)	C(3)	11,130	C(2)	1.113.090	C(4)	1.113.090	Pro-S
H(16)	C(3)	11,130	C(2)	1,138,496	C(4)	1,138,496	Pro-R
H(17)	C(4)	11,130	C(3)	1.113.097	C(5)	1.113.097	Pro-R
H(18)	C(4)	11,130	C(3)	1,138,513	C(5)	1,138,513	Pro-S
H(19)	C(5)	11,130	O(1)	1,110,583	C(4)	1,110,583	Pro-S
H(20)	C(7)	11,130	C(5)	1,094,418	C(8)	1,094,418	Pro-R
H(21)	C(7)	11,130	C(5)	1,094,618	C(8)	1,094,618	Pro-S
H(24)	C(10)	11,130	C(9)	1,094,418	C(11)	1,094,418	Pro-S
H(25)	C(10)	11,130	C(9)	1,094,618	C(11)	1,094,618	Pro-R
H(26)	C(11)	11,130	C(10)	1,094,418	C(12)	1,094,418	Pro-S
H(27)	C(11)	11,130	C(10)	1,094,618	C(12)	1,094,618	Pro-R
H(28)	C(12)	11,130	C(11)	1,094,418	C(13)	1,094,418	Pro-S
H(29)	C(12)	11,130	C(11)	1,094,618	C(13)	1,094,618	Pro-R
H(30)	C(13)	11,130	C(12)	1,094,418	C(14)	1,094,418	Pro-S
H(31)	C(13)	11,130	C(12)	1,094,618	C(14)	1,094,618	Pro-R
H(32)	C(14)	11,130	C(13)	1,095,000	C(12)	1,800,000	Dihedral
H(33)	C(14)	11,130	C(13)	1,094,418	H(32)	1,094,418	Pro-S
H(34)	C(14)	11,130	C(13)	1,094,618	H(32)	1,094,618	Pro-R

Figure 6. Internal coordinate table

Figure 7. Following optimization

2. (Z,Z)-2,5-UNDECADIEN-1-OL

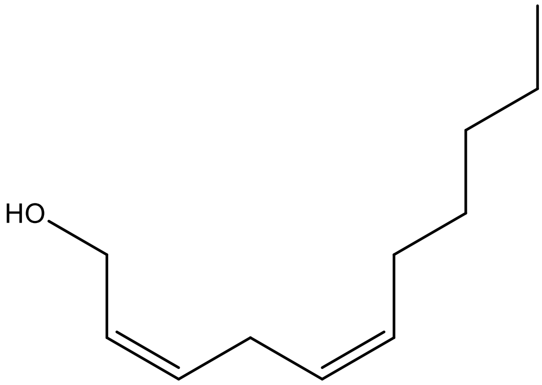


Figure 8. 2 *Z* ,5 *Z*)-undeca-2,5-dien-1-ol

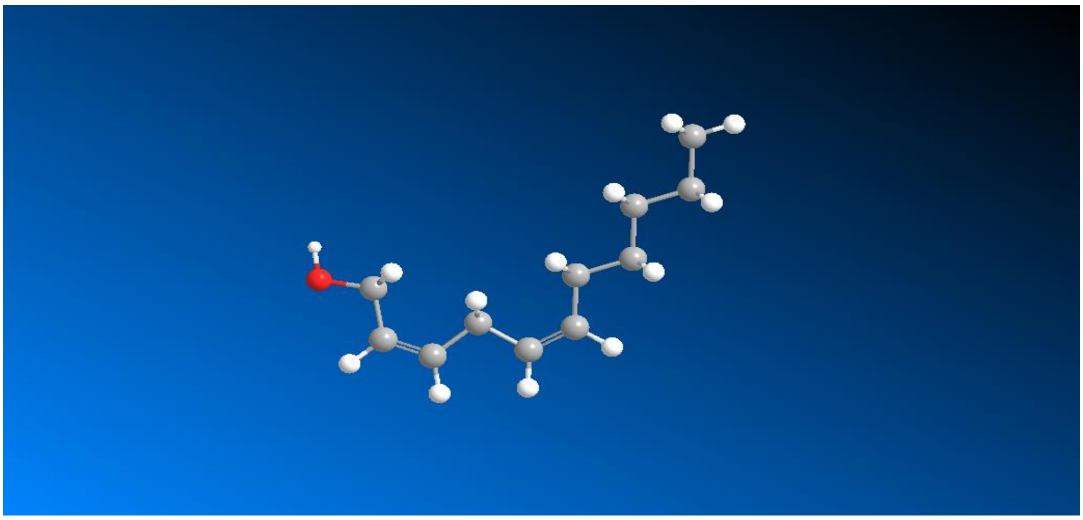


Figure 9. Prior Optimizing

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Atom	X (Å)	Y (Å)	Z (Å)
C(1)	-43,500	-0.7027	00.00
C(2)	-41.061	-21,797	00.00
C(3)	-28,547	-26.505	0
C(4)	-16,976	-17,008	0
C(5)	-0.4161	-24.745	0
C(6)	5.240972	-18,287	0
C(7)	5,44375	-0.3320	0
C(8)	22,293	1.029167	00.00
C(9)	22,590	16,709	00.00
C(10)	37.043	21.511	0
C(11)	37,341	36,738	0
O(12)	-57.302	-0.4563	0
H(13)	-38,932	-0.2518	6.314583
H(14)	-38,928	-0.2513	-0.9088
H(15)	-49,563	-28,776	00.00
H(16)	-26,755	-37.358	0
H(17)	-17,438	-10,605	-0.9092
H(18)	-17.439	-10,599	6
H(19)	-0.4376	-35,743	0
H(20)	16,964	-23.973	0
H(21)	1.854861	0	-0.9092
H(22)	1.851389	0.340278	6,311111
H(23)	27,461	-0.2324	6.314583
H(24)	27,466	-0.2328	-0.9088
H(25)	17,422	20,515	-0.9092
H(26)	17,417	20,519	6
H(27)	42.212	17,705	6
H(28)	42,217	17.701	-0.9088
H(29)	47.903	40,248	0
H(30)	32.173	40,545	-0.9092
H(31)	32.168	40,549	6,311111
H(32)	-58,414	3.327083	00.00

Figure 10. Cartesian Table

Atom	Bond Atom	Bond Length (Å)	Atomic Angle	Angle (°)	2nd Angle Atom	2nd Angle (°)	2nd Angle Type
C(2)							
C(3)	C(2)	13370					
C(1)	C(2)	14,970	C(3)	00.00			

H(15)	C(2)	11,000	C(1)	00.00	C(3)	1,200,000	Pro-R
C(4)	C(3)	14,970	C(2)	00.00	C(1)	00.00	Dihedral
H(16)	C(3)	11,000	C(2)	00.00	C(4)	1,200,000	Pro-S
C(5)	C(4)	14,970	C(3)	00.00	C(2)	1,800,000	Dihedral
H(17)	C(4)	11,130	C(3)	00.00	C(5)	1,094,418	Pro-S
H(18)	C(4)	11,130	C(3)	00.00	C(5)	1,094,618	Pro-R
C(6)	C(5)	13370	C(4)	00.00	C(3)	-180.0000	Dihedral
H(19)	C(5)	11,000	C(4)	00.00	C(6)	1,200,000	Pro-S
C(7)	C(6)	14,970	C(5)	00.00	C(4)	00.00	Dihedral
H(20)	C(6)	11,000	C(5)	00.00	C(7)	1,200,000	Pro-R
C(8)	C(7)	15,230	C(6)	1,095,000	C(5)	1,800,000	Dihedral
H(21)	C(7)	11,130	C(6)	1,094,418	C(8)	1,094,418	Pro-S
H(22)	C(7)	11,130	C(6)	00.00	C(8)	1,094,618	Pro-R
C(9)	C(8)	15,230	C(7)	00.00	C(6)	1,800,000	Dihedral
H(23)	C(8)	11,130	C(7)	1,094,418	C(9)	1,094,418	Pro-S
H(24)	C(8)	11,130	C(7)	1,094,618	C(9)	1,094,618	Pro-R
C(10)	C(9)	15,230	C(8)	00.00	C(7)	1,800,000	Dihedral
H(25)	C(9)	11,130	C(8)	00.00	C(10)	1,094,418	Pro-S
H(26)	C(9)	11,130	C(8)	1,094,618	C(10)	1,094,618	Pro-R
C(11)	C(10)	15,230	C(9)	1,095,000	C(8)	1,800,000	Dihedral
H(27)	C(10)	11,130	C(9)	1,094,418	C(11)	1,094,418	Pro-S
H(28)	C(10)	11,130	C(9)	1,094,618	C(11)	1,094,618	Pro-R
O(12)	C(1)	14,020	C(2)	1,095,000	C(3)	1,800,000	Dihedral
H(13)	C(1)	11,130	C(2)	1,094,418	O(12)	1,094,418	Pro-S
H(14)	C(1)	11,130	C(2)	1,094,618	O(12)	1,094,618	Pro-R
H(29)	C(11)	11,130	C(10)	1,095,000	C(9)	1,800,000	Dihedral

Figure 11. Internal Coordinates

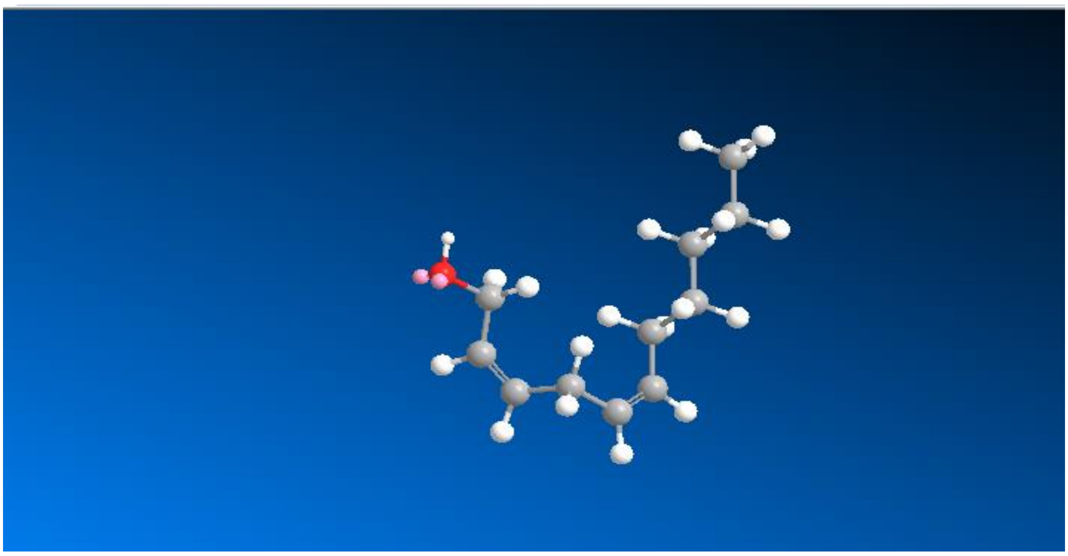

Figure 12. Following optimization

4.2 Discussion

Based on the data analysis, the research conducted can be said to be successful. This can be seen in the active compound contained in Chanoclavine, namely proteases which have a percentage of 33.3 % . Which is a substance dipeptidyl peptidase IV (DPP IV) is associated with diabetes, where it plays a role in inactivating a number of peptides involved in blood sugar balance. This can be used by people with diabetes mellitus, because it can maintain blood sugar levels and provide a faster feeling of fullness when consuming purple sweet potatoes. In addition, the active compounds contained are also able to prevent stress.

5. CONCLUSION

Based on the descriptive results and data analysis on purple sweet potato, 5 active compounds were obtained, namely Chanoclavine, Elymoclavine, Ergine, Ergometrine, and Isoergine. Where in Chanoclavine contains 33.3% proteases, 20% enzymes, 20% chytochrome, 6.7% ligand gated channel, 6.7% electrochemical, 6.7% kinase, and 6.7% Family AG protein coupled receptor. Elymoclavine contains 46.7 % Family AG protein coupled receptors , 26.7% electrochemicals, 6.7% proteases, 6.7% enzymes, 6.7% kinases and 6.7% membrane receptors. Ergometrine contains 93.3% Family AG protein coupled receptor and 6.75 chytochrome . Meanwhile, Ergine and Isoergine only contain Family A G protein coupled receptor with a percentage of 100%.

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REFERENCES

[1] Sumarsih, S., & Hastono, SP (2021). Body Mass Index, Age , and Increased Total Cholesterol Levels. *Metro Sai Wawai Journal of Health* , *13* (1), 44-50.

[2] Hastuty, YD (2018). Differences in cholesterol levels of obese people with non-obese people. *AVERROUS: Malikussaleh Journal of Medicine and Health* , *1* (2), 47-55.

[3] Naim, MR, Sulastri, S., & Hadi, S. (2019). An overview of the results of examination of cholesterol levels in patients with hypertension at the Sheikh Yusuf Hospital, Gowa Regency. *Journal of Laboratory Media* , *9* (2), 33-38.

[4] SATRIANAWATY, LD, MARTINI, T., & PRABOWO, S. (2019). Effect of Moringa Leaf Extract on HDL Cholesterol Levels in Hyperglycemic Male White Rats with Alloxan Induction. *Hang Tuah Medical Journal* , *17* (1), 35-47.

[5] Arifin, AY, Ernawati, F., & Prihatini, M. (2019). The relationship between blood glucose levels and increased blood lipid levels in the cohort study population of Central Bogor sub-district 2018. *Journal of Biotek Medisiana Indonesia* , *8* (2), 87-93.

[6] Tandi, J., Rahmawati, R., Isminarti, R., & Lapangoyu, J. (2018, December). Effects of Pumpkin Seed Extract on Glucose, Cholesterol and Histopathological Appearance of Hypercholesterolemic-Diabetic Mice Pancreas. In *Talenta Conference Series: Tropical Medicine (TM)* (Vol. 1, No. 3, pp. 144-151).

[7] Patala, R., Dewi, NP, & Pasaribu, MH (2020). The effectiveness of ethanol extract of avocado seeds (Persea americana Mill.) on blood glucose levels of male white rats (Rattus novergicus) hypercholesterolemia-diabetic model. *Galenika Journal of Pharmacy (e-Journal)* , *6* (1), 7-13.

[8] Naim, MR, Sulastri, S., & Hadi, S. (2019). An overview of the results of examination of cholesterol levels in patients with hypertension at the Sheikh Yusuf Hospital, Gowa Regency. *Journal of Laboratory Media* , *9* (2), 33-38.

[9] Al-Rahmad, AH (2018). The Effect of Nutrition Counseling on Reducing Blood Cholesterol Levels. *Journal of Health* , *9* (2), 241-247.

[10] Nurazizah, N., Nabila, AI, Adriani, L., Widjastuti, T., & Latipudin, D. (2020). Cholesterol, urea, blood creatinine and cholesterol levels of Sentul chicken eggs with the addition of noni fruit extract supplemented with Cu and Zn . *Journal of Tropical Animal Nutrition and Feed Science* , *2* (1).

[11] Ramadhina, IA, Adriani, L., & Sujana, E. (2019). Effect of administration of kepel leaf extract (Stelechocarpus burahol) on blood cholesterol levels and quail eggs (Coturnix-coturnix japonica). *Journal of Tropical Animal Nutrition and Feed Science* , *1* (1).

[12] Anakonda, S., Widiany, FL, & Inayah, I. (2019). The relationship between exercise activity and cholesterol levels in patients with coronary heart disease. *Indonesian Nutrition Sciences* , *2* (2), 125-132.

[13] Norlita, W., & Wiradinata, DI (2020). The Effect of Cupping Therapy on Cholesterol Levels in Hypercholesterolemic Patients at Thibbun Nabawi Center RSIA Zainab Pekanbaru in 2019. *Photon: Journal of Science and Health* , *10* (2), 125-136.

[14] Khairina, S. (2021). *Effect of ethanol extract of bulian leaf (Eusideroxylon zwageri) on cholesterol levels and liver function in male white mice with diabetes mellitus* (Doctoral dissertation, Pharmacy).

[15] Lysandra, A., Wreksoatmodjo, BR, & Widayanti, JR (2020). RELATIONSHIP OF NON-HDL CHOLESTEROL ON COGNITIVE FUNCTION IN ISCEMIC STROKE PATIENTS WITH A MIDDLE NEUROLOGIC DEFICIT. *Neuroscience Medical Magazine, Indonesian Neurologist Association* , *37* (3).

[16] Ahmad, NH, Irwan, I., Astuty, E., Zulkarnain, Z., Kusadhiani, I., & Hataul, II (2021). The Relationship between Total Cholesterol Ratio and High Density Lipoprotein with the Incidence of Acute Coronary Syndrome in RSUD Dr. M. Haulussy Ambon 2018-2019. *PAMERI: Pattimura Medical Review* , *3* (2), 42-54.

[17] Wijanarko, SI, Herawati, S., & Subawa, AAN (2018). Differences in low density lipoprotein (LDL) cholesterol levels in type 2 diabetes mellitus with hypertension and without hypertension at Sanglah Hospital Denpasar, Bali. *Journal of Medika Udayana* , *7* (3), 117-120.

[18] Rilyani, R., & Kusumaningsih, D. (2019). THE RELATIONSHIP OF SATURATED, NON-UNsaturated fatty acids and fiber with LDL/HDL RATIO IN CORONARY HEART PATIENTS IN HEART POLY OF RSUD Dr. HI. ABDUL MOELOEK. *Holistic Journal of Health* , *10* (4), 221-227.

[19] Sufiati Bintanah, M. (2021). Petul Flour Formula to Improve Nutritional Status and Total Cholesterol in Menopausal Women with Hypercholesterolemia. *Unimus Journal of Nutrition Vol* , *10* (1).

[20] Najiyah, F., Masfufah, A., Fahmi, NF, & Izzati, YMP (2020). ANALYSIS OF HDL LEVELS IN ADULTS OF ACTIVE SMOKERS AGED 31-35 YEARS IN RT. 04. RW. 01 KELURAHAN MLAJAH BANGKALAN. *MEDICAL JOURNAL P-ISSN: 2685-7960 e-ISSN: 2685-7979* , *2* (2), 29-33.

[21] Zainul, R. (2015). Study of Pb (II) biosorption from aqueous solution using immobilized Spirogyra subsalsa biomass. *Journal of Chemical and Pharmaceutical Research* , *11* (7), 715-722.

[22] Adri, M., Zainul, R., Wahyuningtyas, N., Wedi, A., Surahman, E., Aisyah, E. N. , ... & Adnan, E. (2020, July). Development of Content Learning System in Professional Education Subjects for Educational Institutions in Indonesia. In *Journal of Physics: Conference Series* (Vol. 1594, No. 1, p. 012022). IOP Publishing.

[23] Rais, NSM, Isa, IM, Hashim, N., Saidin, MI, Yazid, SNAM, Ahmad, M. S. , ... & Mukdasai, S. (2019). Simultaneously Determination of Bisphenol A and Uric Acid by Zinc/Aluminum-layered Double

Hydroxide-2-(2, 4dichlorophenoxy) Propionate Paste Electrode. *International Journal of ELECTROCHEMICAL SCIENCE* , *14* , 7911-7924.

[24] Zainul, R. (2015). Study of Pb (II) biosorption from aqueous solution using immobilized Spirogyra subsalsa biomass. *Journal of Chemical and Pharmaceutical Research* , *11* (7), 715-722.

[25] Rais, NSM, Isa, IM, Hashim, N., Saidin, MI, Yazid, SNAM, Ahmad, M. S. , ... & Mukdasai, S. (2019). Simultaneously Determination of Bisphenol A and Uric Acid by Zinc/Aluminum-layered Double Hydroxide-2-(2, 4dichlorophenoxy) Propionate Paste Electrode. *International Journal of ELECTROCHEMICAL SCIENCE* , *14* , 7911-7924.

[26] Anhar, A., Sumarmin, R., & Zainul, R. (2016). Measurement of glycemic index of West Sumatra local rice genotypes for healthy food selection. *Journal of Chemical and Pharmaceutical Research* , *8* (8), 1035-1040.

[27] Zainul, R. (2016). Effect of Temperature and Particle Motion against the ability of ZnO Semiconductor Photocatalyst in Humic Acid. *Der Pharmacia Lettre* , *15* (8), 120-124.

[28] Tamarani, A., Zainul, R., & Dewata, I. (2019, April). Preparation and characterization of XRD nano Cu-TiO2 using sol-gel method. In *Journal of Physics: Conference Series* (Vol. 1185, No. 1, p. 012020). IOP Publishing.

[29] Kurniawati, D., & Zainul, R. (2015). Biosorption of Pb (II) from aqueous solutions using column method by longan (Euphoria logan lour) seed and shell. *Journal of Chemical and Pharmaceutical Research* , *7* (12), 872-877.

[30] Putri, GE, Arief, S., Jamarun, N., Gusti, FR, & Zainul, R. (2019). Microstructural analysis and optical properties of nanocrystalline cerium oxides synthesized by precipitation method. *Rasayan J. Chem* , *12* (1), 85-90.