Uluslararası İleri Doğa Bilimleri ve Mühendislik Araştırmaları Dergisi
Sayı 8, S. 293-303, 2, 2024

Araştırma Makalesi

IJANSER
https://as-proceeding.com/index.php/ijanser
ISSN: 2980-0811

International Journal of Advanced Natural Sciences and Engineering Researches
Volume 8, pp. 293-303, 2, 2024

Research Article

A study on investigation of the inhibition effects of some effective compounds for CD36 and LDL in atherosclerosis by using chemical computation method

Faik Gökalp1*

[1] *Kırıkkale University, Faculty of Education, Science Education, Turkiye.*
Email of corresponding author: akgokalp@gmail.com

(Received: 08 March 2024, Accepted: 12 March 2024)

(4th International Conference on Innovative Academic Studies ICIAS 2024, March 12-13, 2024)

ATIF/REFERENCE: Gökalp, F. (2024). A study on investigation of the inhibition effects of some effective compounds for CD36 and LDL in atherosclerosis by using chemical computation method. *International Journal of Advanced Natural Sciences and Engineering Researches, 8(2), 293-303.*

Abstract – Aronia melanocarpa belongs to the Rosaceae family and is a shrub-shaped plant. Aronia fruits, which are an important food source with their dark colored fruits and are also used in traditional medicine, are also very rich in anthocyanins, flavonols and phenolic acids. Rich in polyphenols such as anthocyanins, procyanidins and flavonoids.

The effects of aronia on inhibiting the progression of atherosclerotic plaque are being investigated. LDL (low-density lipoprotein), which is synthesized in the liver and transported through the blood and is an important parameter in determining the risk of heart disease, is a harmful form of cholesterol that contributes to the development of atherosclerosis, a condition that can lead to heart attack through plaque formation in the arteries. In the early stage of atherosclerosis, CD36 is essential, serving as a pattern recognition receptor for non-classical monocyte functions through monitoring patrol activity and mediating free fatty acid transport to hematopoietic stem cells in response to infections. In this study, the interaction of CD36 and LDL, which have important roles in atherosclerosis, with natural active compounds determined and selected through literature research using the chemical calculation method, will be investigated. The data obtained is important in terms of providing direction for experimental and clinical studies in this field by preventing loss of time and material.

Keywords – Aronia, Anthocyanin, Atorvastatin, Atherosclerosis, CD36, LDL, Hydroxycinnamic Acid.

[1] * Associate Professor Faik Gökalp also conducts research studies at Iğdır University Faculty of Health Sciences

I. INTRODUCTION

Aronia melanocarpa, is a fruit native to North America and used as food by indigenous peoples to prevent chronic diseases (1). A study has shown that atherosclerotic plaques as oxidized LDL facilitate the formation of lipid-laden foam cells in the artery, which are the hallmark of early atherosclerotic disease. (2). Aronia Melanocarpa is a plant rich in flavonoids and anthocyanides (3). Some of these are natural compounds such as hydroxycinnamic acid, flavanols, and anthocyanin. (4-6).
Atherosclerotic cardiovascular disease is the leading cause of morbidity and mortality worldwide (7). Atherosclerosis is a serious condition characterized by disruption and apoptosis of endothelial cells and dysfunction of vascular smooth muscle cells with persistent systemic and focal inflammation (8). Atorvastatin reduces LDL-cholesterol levels in patients and is a safe and effective HMG-CoA reductase inhibitor (9,10).
In this study, the interactions of ligands, which are some natural active ingredients in aronia effective for atherosclerosis, with LDL and CD36 receptors were investigated using docking, a chemical calculation method.

II. MATERIAL AND METHOD

The interaction of CD36 and LDL receptors, which have an important role in atherosclerosis, and ligands, which are some naturally effective compounds in aronia, will be tried to elucidate the mechanism of ligand-receptor interactions that will guide experimental and clinical studies, by using docking (11-14), a chemical calculation method that provides data very close to the results obtained from experimental studies.

III. RESULTS AND DİSCUSSİON

The interaction docking scores of some important active substances in Aronia with the CD36 receptor, which has important roles in atherosclerosis as ligands, are given in Table 1 .

Table 1. The interaction docking scores of some important active substances in Aronia with the CD36 receptor, which has important roles in atherosclerosis as ligands

Docking scores of Ligands / Reseptör (CD36)	**Free Energy of Binding (kcal/mol)**	**Inhibition Constant, Ki**	
Atorvastatin	-4.67	380.24	uM
Antosiyanins	-3.90	1.39	mM
Hydroxycinnamic acid	-2.84	8.26	mM

In Table 1, when the interactions of the ligands determined according to docking scores and Ki values with the CD36 receptor, which has important roles in atherosclerosis, are listed from largest to smallest; Atorvastatin > Anthocyanins > Hydroxycinnamic acid. As an effective drug ligand, the intermolecular bonds formed as a result of the interaction of atorvastatin with the CD36 receptor, which has important roles in atherosclerosis, are given in Table 2 (11-14).

Table 2. The intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of atorvastatin with the CD36 receptor in atherosclerosis as an effective drug ligand.

hydrogen bonds	polar	cation-pi	other
TRP66 (-3.6693)	GLU366 (11.8011)	TRP415 (-2.3906)	ARG386 (-3.4293)
			ASN417 (-1.8984)
			GLN87 (-1.3027)
			GLU365 (-1.2674)
			ASN363 (-1.2066)
			PRO90 (-0.3592)

As an effective drug ligand, the hydrogen bond formed by the interaction of atorvastatin with the CD36 receptor in atherosclerosis is given in Figure 1(11-14) .

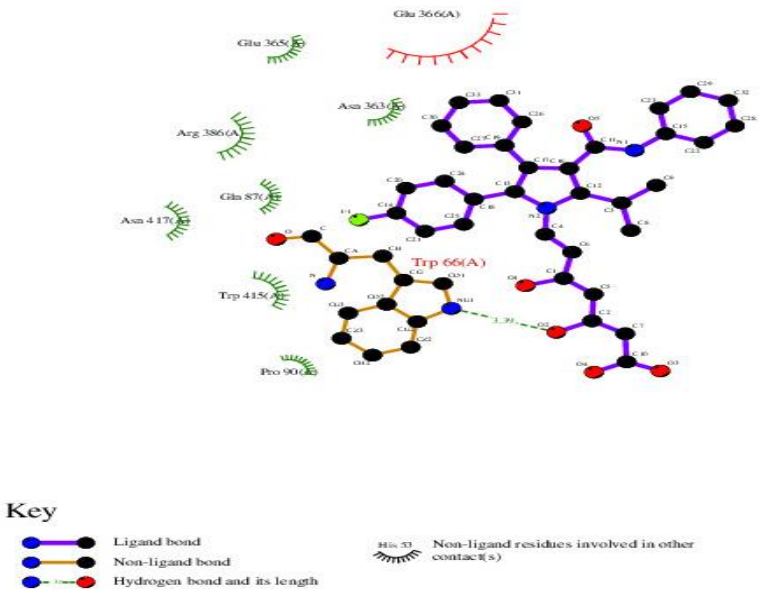

Figure 1. Hydrogen bond formation of Atorvastatin as an effective drug ligand as a result of its interaction with the CD36 receptor in atherosclerosis

As an effective drug ligand, atorvastatin's interaction points with the CD36 receptor in atherosclerosis are given in Figure 2 (11-14) .

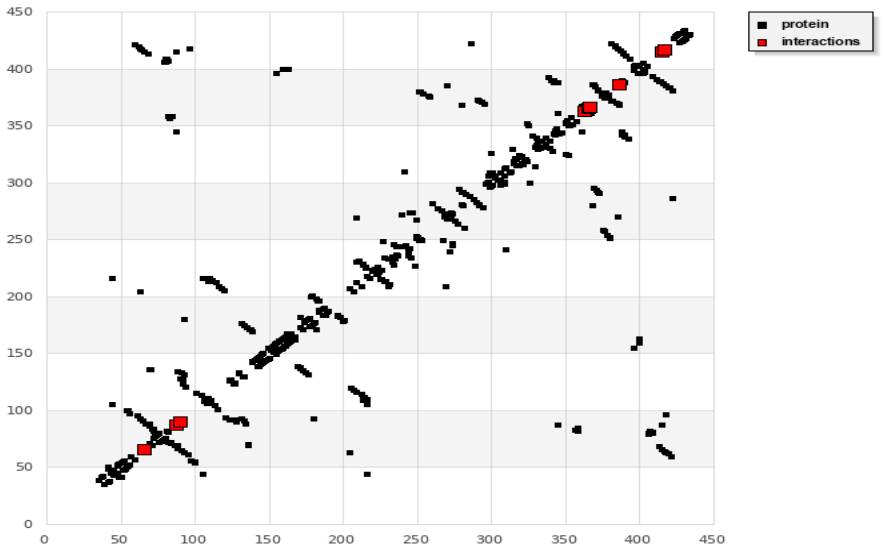

Figure 2. Atorvastatin, as an effective drug ligand, interacts with the CD36 receptor in atherosclerosis.

In Figure 2, the interaction points of Atorvastatin as an effective drug ligand with the CD36 receptor in atherosclerosis: 66: TRP87: GLN90: PRO363: ASN365: GLU366: GLU386: ARG415: TRP417: ASN.

The intermolecular bonds formed as a result of the interaction of anthocyanin with the CD36 receptor, which has important roles in atherosclerosis as an effective ligand, are given in Table 3 (11-14) .

Table 3. The intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of anthocyanin with the CD36 receptor in atherosclerosis as an effective ligand.

hydrophobic	**other**
TYR62 (-1.4058)	THR92 (-0.8394)
LEU126 (-0.6491)	THR421 (-0.4367)
	THR419 (-0.4003)
	GLN64 (0.912)

As an effective ligand, anthocyanin interaction points with the CD36 receptor in atherosclerosis are given in Figure 3 (11-14) .

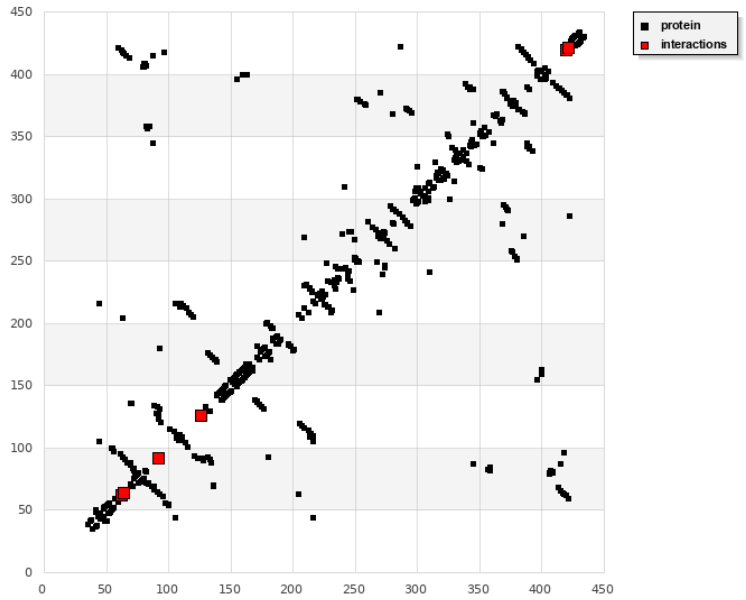

Figure 3. The interaction points of anthocyanin with the CD36 receptor in atherosclerosis as an effective ligand

In Figure 3, Anthocyanin interaction points with CD36 receptor in atherosclerosis as an effective ligand: 62: TYR64: GLN92: THR126: LEU419: THR421: THR.

As an effective ligand, hydroxycinnamic acid, the intermolecular bonds formed as a result of its interaction with the CD36 receptor, which has important roles in atherosclerosis, are given in Table 4 (11-14) .

Table 4. The intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of Hydroxycinnamic acid with the CD36 receptor in atherosclerosis as an effective ligand.

hydrogen bonds	**polar**	**hydrophobic**	**other**
ARG386 (-0.6262)	TRP66 (-1.4525)	TRP415 (-0.6142)	GLU366 (-0.6864)
	ASN417 (-0.4527)		GLN87 (-0.2368)

The hydrogen bond formed as a result of the interaction of Hydroxycinnamic acid with the CD36 receptor in atherosclerosis, as an effective drug ligand, is given in Figure 4 (11-14) .

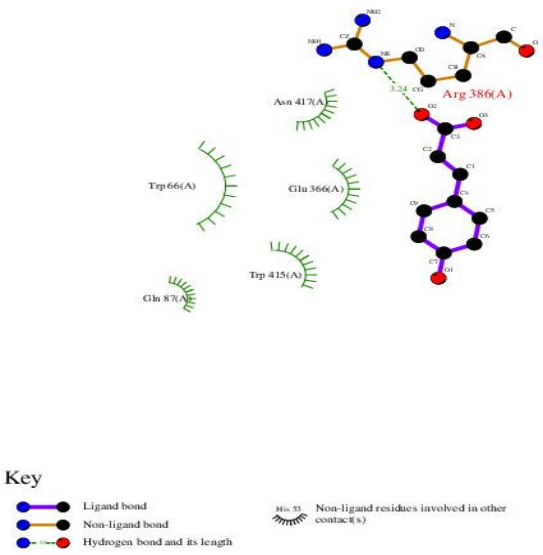

Figure 4. Hydroxycinnamic acid as an effective drug ligand, hydrogen bond formed as a result of its interaction with the CD36 receptor in atherosclerosis

As an effective ligand of hydroxycinnamic acid, its interaction points with the CD36 receptor in atherosclerosis are given in Figure 5 (11-14) .

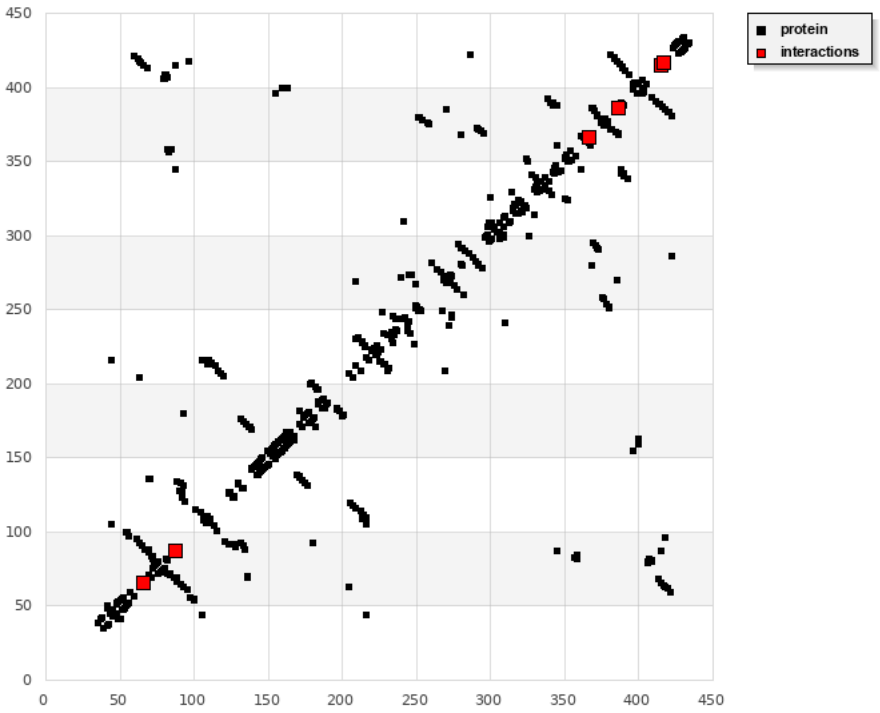

Figure 5. Hydroxycinnamic acid, as an effective ligand, interacts with the CD36 receptor in atherosclerosis

In Figure 5, Hydroxycinnamic acid, as an effective ligand, interacts with the CD36 receptor in atherosclerosis: 66: TRP87: GLN366: GLU386: ARG415: TRP417: ASN.

The interaction docking scores of some important active ingredients in Aronia with the LDL receptor, which has important roles in atherosclerosis as ligands, are given in Table 5 (11-14).

Table 5. The interaction docking scores of some important active substances in Aronia with LDL receptor, which has important roles in atherosclerosis as ligands

Docking scores of Ligands / ReseptörFree Energy of Binding (kcal/mol) (LDL)		Inhibition Constant, Ki
Atorvastatin	-2.87	7.92 mM
Antosiyanins	-5.13	172.21 uM
Hydroxycinnamic acid	-2.25	22.53 mM

In Table 5, when the interactions of the ligands determined according to docking scores and Ki values with the LDL receptor, which has important roles in atherosclerosis, are listed from largest to smallest; Anthocyanins > Atorvastatin > Hydroxycinnamic acid. The intermolecular bonds formed as a result of the interaction of atorvastatin with the LDL receptor, which has important roles in atherosclerosis as an effective drug ligand, are given in Table 6 (11-14).

Table 6. Intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of atorvastatin with the LDL receptor in atherosclerosis as an effective drug ligand.

halogen-bond	hydrophobic	other
GLN133 (-0.6032)	PHE132 (-1.4857)	ASN135 (-1.2907)
		CYS163 (-0.4336)
		ARG162 (-0.2873)
		CYS146 (-0.1342)

As an effective drug ligand, the hydrogen bond formed by the interaction of atorvastatin with the LDL receptor in atherosclerosis is given in Figure 6 (11-14) .

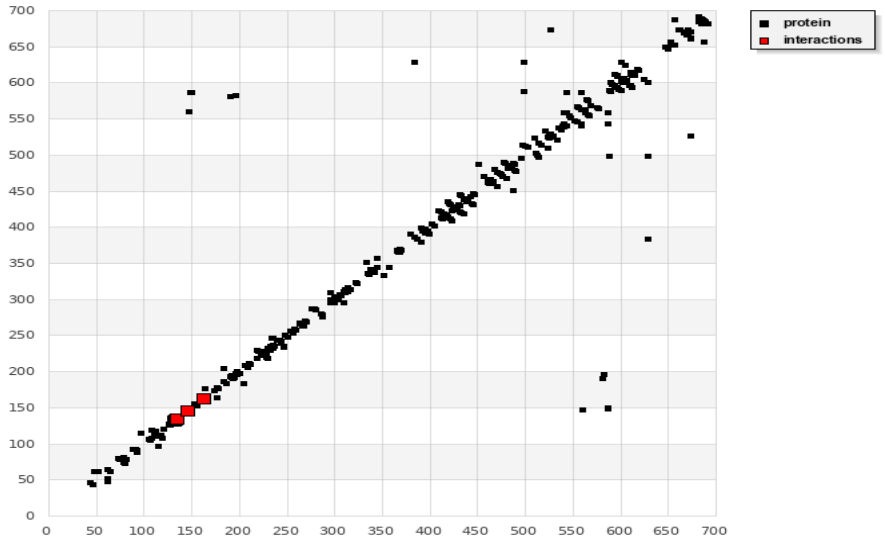

Figure 6. Atorvastatin, as an effective drug ligand, interacts with the LDL receptor in atherosclerosis

In Figure 6, Atorvastatin interaction points with LDL receptor in atherosclerosis as an effective drug ligand: 132: PHE133: GLN135: ASN146: CYS162: ARG163: CYS.

The intermolecular bonds formed as a result of the interaction of anthocyanin with the LDL receptor, which has important roles in atherosclerosis as an effective ligand, are given in Table 7 (11-14) .

Table 7. The intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of anthocyanin with the LDL receptor in atherosclerosis as an effective ligand.

hydrophobic	**other**
PHE132 (-2.5329)	GLN133 (-1.2304)
CYS127 (-0.3095)	ASN135 (-0.7132)
	SER131 (-0.2282)
	GLN161 (-0.1666)

As an effective ligand, anthocyanin's interaction points with the LDL receptor in atherosclerosis are given in Figure 7 (11-14) .

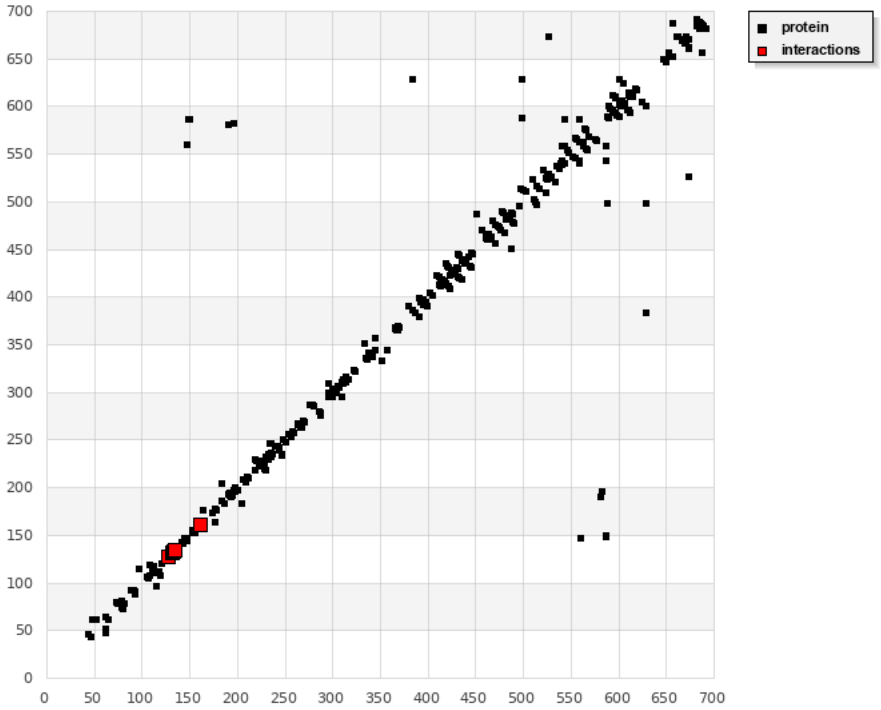

Figure 7. Anthocyanin interaction points with LDL receptor in atherosclerosis as an active ligand

In Figure 7, Anthocyanin interaction points with LDL receptor in atherosclerosis as an effective ligand: 127: CYS131: SER132: PHE133: GLN135: ASN161: GLN.

The intermolecular bonds formed as a result of the interaction of Hydroxycinnamic acid with the LDL receptor, which has important roles in atherosclerosis as an effective ligand, are given in Table 8 (11-14) .

Table 8. The intermolecular bonds and energy values (kcal/mol) formed as a result of the interaction of Hydroxycinnamic acid with the LDL receptor in atherosclerosis as an effective ligand.

hydrogen bonds	**polar**	**hydrophobic**	**other**
SER131 (-0.1733)	GLN133 (-1.2422)	PHE132 (-2.2285)	GLN161 (-0.19)
	ASN135 (-0.741)	CYS127 (-0.1735)	

The hydrogen bond formed as a result of the interaction of Hydroxycinnamic acid with the LDL receptor in atherosclerosis, as an effective ligand, is given in Figure 8 (11-14).

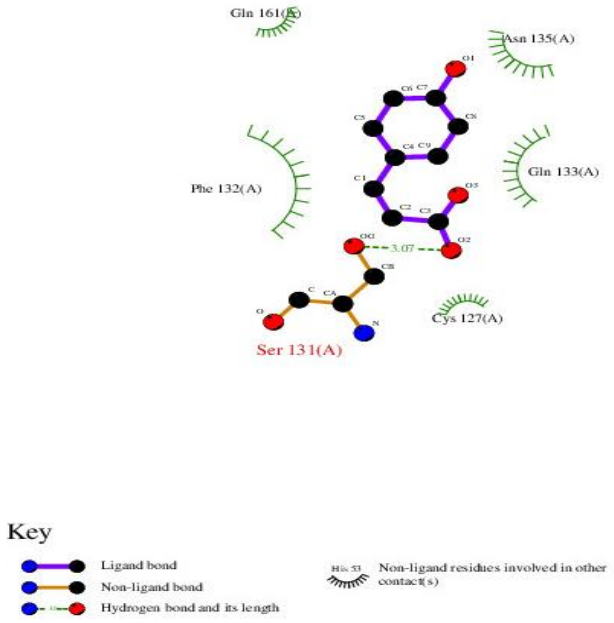

Figure 8. Hydroxycinnamic acid as an effective ligand, hydrogen bond formed as a result of its interaction with the LDL receptor in atherosclerosis

As an effective ligand of hydroxycinnamic acid, its interaction points with the LDL receptor in atherosclerosis are given in Figure 9 (11-14).

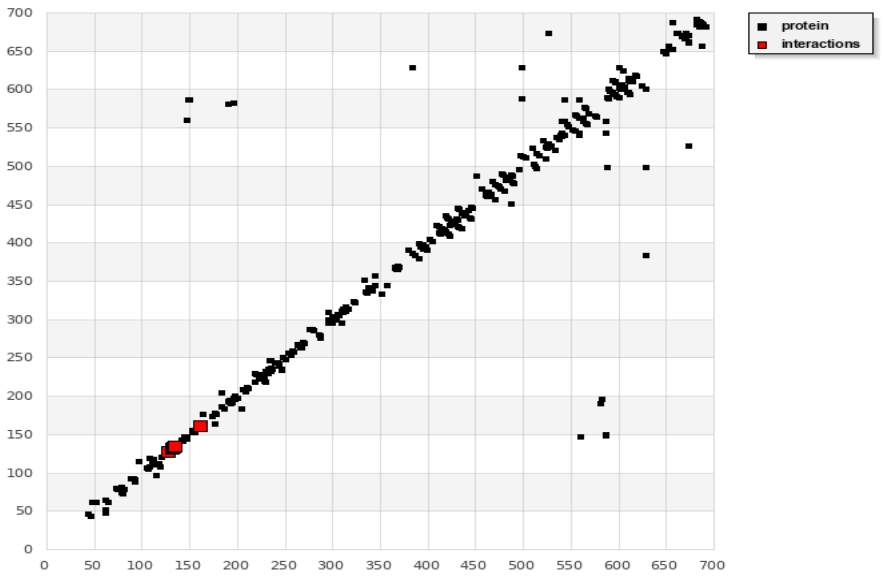

Figure 9. Hydroxycinnamic acid, as an effective ligand, interacts with the LDL receptor in atherosclerosis

In Figure 9, Hydroxycinnamic acid, as an effective ligand, interacts with the LDL receptor in

atherosclerosis: 127: CYS131: SER132: PHE133: GLN135: ASN161: GLN.

It is very important to determine the intermolecular bonds and interaction points in order to see the interactions of the identified receptors and the selected ligands, and the studies (15-19) on understanding the mechanism of action of intermolecular bonds and determining the interaction points support this study.

IV. CONCLUSION

The intermolecular bonds and interaction points that may be formed by the interaction of CD36 and LDL receptors, which have an important role in atherosclerosis, with the ligands of some active substances in aronia, were investigated using the chemical calculation method. Among these active ingredients, Anthocyanins and Hydroxycinnamic acid, when compared to the reference drug active ingredient Atorvastatin, it is understood that Anthocyanin is very effective for CD36 and Anthocyanin is more effective for LDL. The data obtained here is important in terms of guiding experimental and clinical studies by preventing loss of time and material.

REFERENCES

1.Brunelle, D. C., Larson, K. J., Bundy, A., Roemmich, J. N., Warne, D., & Redvers, N. (2024). Chokeberry reduces inflammation in human preadipocytes. *Journal of Functional Foods*, *112*, 105947.

2.Kim, B., Ku, C. S., Pham, T. X., Park, Y., Martin, D. A., Xie, L., ... & Bolling, B. W. (2013). Aronia melanocarpa (chokeberry) polyphenol–rich extract improves antioxidant function and reduces total plasma cholesterol in apolipoprotein E knockout mice. *Nutrition Research*, *33*(5), 406-413.

3.Eryaman, Z., Hizal, J., Yılmazoğlu, M., Daban, U., Mert, H., & Kanmaz, N. (2024). The performance of hypochlorous acid modified Ag nanoparticle-based assay in the determination of total antioxidant capacity of Boswellia Serrata and Aronia. *Talanta*, *267*, 125218.

4.Nhuan Do Thi1 and Eun-Sun Hwang,Bioactive Compound Contents and Antioxidant Activity in Aronia (Aronia melanocarpa) Leaves Collected at Different Growth Stages,Prev. Nutr. Food Sci. 2014;19(3):204-212

5. Sharif T, Stambouli M, Burrus B, Emhemmed F, Dandache I, Auger C, Etienne-Selloum N, Schini-Kerth VB, Fuhrmann G. 2013. The polyphenolic-rich Aronia melanocarpa juice kills stereotocarcinomal cancer stem-like cells, but not their differentiated counterparts. J Funct Foods 5: 1244-1252

6. Malinowska J, Babicz K, Olas B, Stochmal A, Oleszek W. 2012. Aronia melanocarpa extract suppresses the biotoxicity of homocysteine and its metabolite on the hemostatic activity of fibrinogen and plasma. Nutrition 28: 793 -798.

7.Zheng, W. C., Chan, W., Dart, A., & Shaw, J. A. (2024). Novel therapeutic targets and emerging treatments for atherosclerotic cardiovascular disease. *European Heart Journal-Cardiovascular Pharmacotherapy*, *10*(1), 53-67.

8.Pan, Q., Chen, C., & Yang, Y. J. (2024). Top five stories of the cellular landscape and therapies of atherosclerosis: current knowledge and future perspectives. *Current Medical Science*, *44*(1), 1-27.

9. Malhotra, H. S., & Goa, K. L. (2001). Atorvastatin: an updated review of its pharmacological properties and use in dyslipidaemia. *Drugs*, *61*(12), 1835-1881.

10. Black, D. M., Bakker-Arkema, R. G., & Nawrocki, J. W. (1998). An overview of the clinical safety profile of atorvastatin (lipitor), a new HMG-CoA reductase inhibitor. *Archives of internal Medicine*, *158*(6), 577-584.

11. Bikadi, Z., Hazai, E.*Application of the PM6 semi-empirical method to modeling proteins enhances docking accuracy of AutoDock*J. Cheminf. **1**, 15 (2009)

12. Huey, R., Morris, G. M., Olson, A. J. and Goodsell, D. S.*A Semiempirical Free Energy Force Field with Charge-Based Desolvation*J. Comput. Chem. **28**, 1145-1152 (2007)

13.Bikadi,Z. Demko, L. and Hazai, E. (2007) *Functional and structural characterization of a protein based on analysis of its hydrogen bonding network by hydrogen bonding plot*Arch. Biochem. Biophys. **461**, 225-234.

14. McDonald I. K. and Thornton J. M. (1994) *Satisfying Hydrogen Bonding Potential in Proteins*JMB **238**, 777-793.

15.Karakaya, M. F., Gökalp, F., Sener, E., & Korkmaz, O. T. (2023). Investigation of the Pharmacokinetic Properties and Theoretical Chemical Activities of 7, 8-Dihydroxyflavone and 4'-Dimethylamino-7, 8-Dihydroxyflavone. *Current Pharmaceutical Analysis*, *19*(4), 317-323.

16.Gökalp, F. (2024). An investigation into the usage of black cumin derivatives against cancer and COVID-19 as the nature medicine. *Journal of Biomolecular Structure and Dynamics*, 1-8.

17. Gökalp, F. (2022). The curative effect of some natural active compounds for liver cancer. *Medical Oncology*, *40*(1), 57.
18. Gökalp, F. (2022). An Investigation into the Usage of Monosaccharides with GLUT1 and GLUT3 as Prognostic Indicators for Cancer. *Nutrition and Cancer*, *74*(2), 515-519.
19. Gökalp, F. (2020). The inhibition effect of natural food supplement active ingredients on TP63 carcinoma cell. *Medical Oncology*, *37*(12), 120.