THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023), Issue 4, p.71-76

DOI: https://doi.org/10.56936/18290825-2023.17.f-71

# IN-SILICO DOCKING ANALYSIS OF SELECTED FLAVONOIDS AND PROTECTIVE ANTIGEN

**Bakhtari A.[1]*, Gavanji S.[2]**

[1] Department of Reproductive Biology, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

[2] Department of Plant Biotechnology, Medicinal Plants Research Centre, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran

*Received 09.09.2023; Accepted for printing 08.10.2023*

***Abstract***

*Anthrax toxin released by virulent strains of the bacterium, Bacillus anthracis, plays key factor in anthrax disease.*

*The main purpose of this study was to investigate the interaction between four flavonoid ligands including Rhamnetin, Apigenin, Tectochrysin, Pinocembrin and protective antigens.*

*Bioinformatics checking was done by means of Molegro virtual docker and Chimera 1.7. Also, in order for more accuracy, servers like Swiss Dock and BSP-SLIM, and all outputs obtained from this software were compared with each other. The results demonstrated that Apigenin interacted with the Glu117 which is crucial part of binding to its ligand with -12.3453 kca/mol. Also, the highest Fullfitness among these four ligands attributed to Rhamnetin with -994.80 kcal/mol and the ΔG =-7.06 kcal/mol.*

*Results demonstrated that every four ligands possessed interaction with protective antigen and so have inhibitory effect on its interaction with cell membranes but the inhibitory activity of Apigenin and Rhamnetin in interaction is stronger than others flavonoids. Results shown above bring up laboratory studies based on these flavonoids in order to produce an efficacious drug against anthrax.*

***Keywords:*** *Rhamnetin, Apigenin, Tectochrysin, Pinocembrin, protective antigens, Willebrand factor*

## Introduction

Anthrax, charbon (France), Milzbrand (Germany) is derived from Greek anthrakos, meaning coal, emanating from the black color of the eschar in the human skin. Bacillus anthracis (so named by Cohn in 1875) is agent for anthrax which is peracute, acute or subacute disease involving a broad range of animal including humans, mammals and even birds [*Turnbull P, 2002*] it can occur generally in three forms cutaneous anthrax, gastrointestinal anthrax and inhalational anthrax [*Nickell Z, Moran M, 2017*] leading not only to high mortality rate also indirectly can affect Gross national product [*Siamudaala V et al., 2006*]. Lack of accurate controlling system and difficulty of counting number of infected people throughout the world contributes to lack of precise evaluation. The distribution of anthrax is now in agricultural regions of South and Central America, sub-Saharan Africa, central and southwestern Asia, and southern and eastern Europe [*Sitali D et al., 2017*]. Etiological

***Cite This Article as:***

Bakhtari A., Gavanji S. *(2023);* In-silico docking analysis of selected flavonoids and protective antigen; The New Armenian Medical Journal, vol.17(3), p 71-76; DOI: https://doi.org/10.56936/18290825-2023.17.f-71

***Address for Correspondence:***

Azizollah Bakhtari, PhD
Department of Reproductive Biology Shiraz University of Medical Sciences, P.O. Box 71345-1583, Shiraz, Iran
Tel.: +989177048963
E-mail: azizollah.bakhtari@gmail.com

agent of anthrax, Bacillus anthracis, is G+ endospore-forming bacterium belonging to the family Bacillaceae and the class Clostridia which is responsible for anthrax. The three proteins that make up anthrax toxin are protective antigen (PA) two enzymes, lethal factor and edema factor. Combination of each part with another lead to produce two distinct reactions in host: protective antigen + lethal factor brings about edema and protective antigen +lethal factor bring about death [*Blaustein R et al., 1989*]. Protective antigen can joint with a membrane receptor and the N-terminal20-kDa domain of PA20 is cut by cellular protease (Furin), relinquishing the C-termina63 -kDa domain to join to the receptor [*Molloy S et al., 1992*]. Elimination of PA20 exposes a site on protective antigen 63 where bind either edema factor or lethal factor. The critical issue occurs when PA is suitable to interact with endosomal membrane in order to the lipid layer to the cytosol [*Milne J et al., 1994*] and consequently can inhibit the neutrophils activity and suppress the immune system [*Collier R, Young J, 2003*]. Nowadays, excessive consumption of antibacterial and antibiotics and the danger of resistance pose a risk to human health [*Dar D, Sorek R, 2017*] result in investigating large number of scholars, introducing and inventing natural poly phenol replaced antibiotics [*Pearson H et al., 2017*]. unfortunately, lack of optimal efficiency, unwanted side effect, high cost of production and lack of guarantee against all source of B. anthracis are the stumbling blocks of current vaccine [*Tournier J et al., 2009; Mushayabasa S et al., 2017*] so, introducing and identifying new natural compound to combat with anthrax is essential part of sustainable program. Propolis, part of defense system substance, releasing from honey bee as an antibacterial and antiseptic

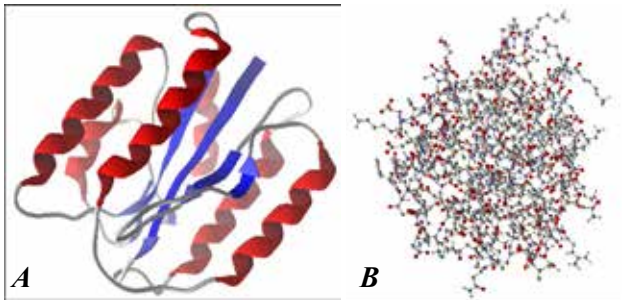



***Figure 1.*** *(A) 3D structure of Protective\(B) Secondary structure of Protective Antigen (PA)*

agent in hive [*Simone-Finstrom M et al., 2017*]. In addition, anticancer [*Pang S et al., 2017*] antioxidant [*Ferreira J et al., 2017*] and anti-septic effect especially in implant operation is proven in human . The primary aim of this study was to investigate the inhibitory effect of propolis flavonoid on protective antigen interaction based on bioinformatics methods.

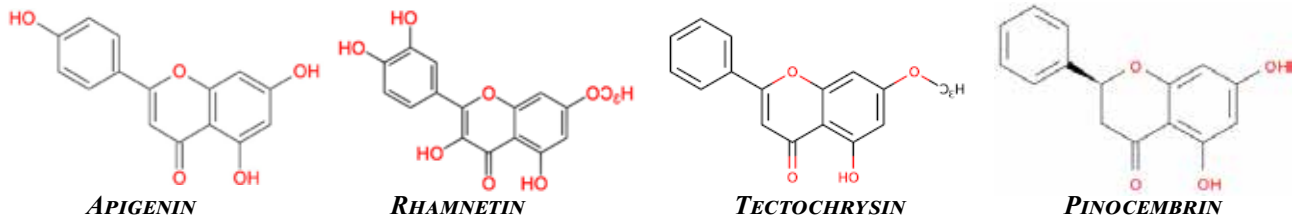
## *Material and methods*

### (Crystal Structure of the von Willebrand factor A domain of human capillary morphogenesis protein 2: an anthrax toxin receptor)

The 3D structure of receptor was derived from Protein Data Bank at www.rcsb.org with 1SHT number (Fig. 1). This web source is a complete source of information making up more than one hundred of biological macromolecule 3D structures such as protein and nucleic acids. The sequence of Amino acid of receptor and its own identification number extracted from NCBI web site) and also identification number P13423 of 3D structure is delineated in figure 2. Four out of all propolis components were selected as ligand to more investigate, then the 3D structure of them was obtained from www.zinc.docking.org and www.chemspider.com (Fig. 3).

MKKRKVLIPLMALSTILVSSTGNLEVIQAEVKQENRLLNESESSSQGLLGYYFSDLNFQAPMVVTSSTTGDLS
IPSSELENIPSENQYFQSAIWSGFIKVKKSDEYTFATSADNHVTMWVDDQEVINKASNSNKIRLEKGRLYQIKI
QYQRENPTEKGLDFKLYWTDSQNKKEVISSDNLQLPELKQKSSNSRKKRSTSAGPTVPDRDNDGIPDSLEVE
GYTVDVKNKRTFLSPWISNIHEKKGLTKYKSSPEKWSTASDPYSDFEKVTGRIDKNVSPEARHPLVAAYPIVH
VDMENIILSKNEDQSTQNTDSQTRTISKNTSTSRTHTSEVHGNAEVHASFFDIGGSVSAGFSNSNSSTVAIDHS
LSLAGERTWAETMGLNTADTARLNANIRYVNTGTAPIYNVLPTTSLVLGKNQTLATIKAKENQLSQILAPNNY
YPSKNLAPIALNAQDDFSSTPITMNYNQFLELEKTKQLRLDTDQVYGNIATYNFENGRVRVDTGSNWSEVLP
QIQETTARIIFNGKDLNLVERRIAAVNPSDPLETTKPDMTLKEALKIAFGFNEPNGNLQYQGKDITEFDFNFDQ
QTSQNIKNQLAELNATNIYTVLDKIKLNAKMNILIRDKRFHYDRNNIAVGADESVVKEAHREVINSSTEGLLL
NIDKDIRKILSGYIVEIEDTEGLKEVINDRYDMLNISSLRQDGKTFIDFKKYNDKLPLYISNPNYKVNVYAVKE
NTINPSENGDTSTNGIKKILIFSKKGYEIG

***Figure 2.*** *Amino acid sequence of anthrax protective antigen in NCBI*




***Apigenin*** ***Rhamnetin*** ***Tectochrysin*** ***Pinocembrin***

***Figure 3.*** *Structure of ligands*

The interaction between each ligand and its receptor was investigated based on Swissdock web server at www.swissdock.ch. This web server was established in order for online studying of interaction between ligands and proteins acting according to EADock DSS. First, the three-dimensional structure of protein or the issue number of protein and ligand should be given. The duration time of docking depends on the size of protein and ligand. The results of docking demonstrated Fullfitness as a number indicative of interaction and Estimated ΔG as an energy. The higher negative score is indicative of stronger interaction between protein and ligands [*Mohammadi E et al., 2017*]. After finding of appropriate ligand for each receptor, identifying of the appropriate amino acid agent in joining process was done by means of Chimera software (UCSF Chimera Version 1.7) chimera isextensible programfor analyzing molecular structure according to their density maps, supramolecular assemblies, sequence alignments, docking results, trajectories, and conformational ensembles.The results of docking demonstrated Fullfitness as a number indicative of interaction and Estimated ΔG as an energy. The greater negative score is indicative of stronger interaction between protein and ligands (www.cgl.ucsf.edu/chimera) [*Saedi Z et al., 2017*].

### Results

Analyzing of data used by SwissDock web server was indicated of compound interacting with receptor with apt energy (Table 1). The results pertained to interaction of ligand and Protective antigen used by SwissDock web server demonstrated that the highest fulfitness was refered to Rhamnetin with ΔG= *kcal/moll* -7.06 and Fullfitness= -994.80 *kcal/moll* then Apigenin ΔG= -6.22 *kcal/moll* and Fullfitness= - 947.67 *kcal/moll* Tectochrysin ΔG= -6.59 *kcal/moll* -7.06 and Fullfitness= -930.25 *kcal/moll* Pinocembrin ΔG -7.08 *kcal/moll* -7.06 and Fullfitness= -912.4 *kcal/moll*. The comparison of interaction by BSP-SLIM server (http://zhanglab.ccmb.med.umich.edu/BSP-SLIM) asserted that the greatest interaction was in Rhamnetin, Tectochrysin, Apigenin and Pinocembrin (Table 2). The results of interaction between ligands and Protective antigen (http://zhanglab.ccmb.med.umich.edu/BSP-SLIM) asserted that Apigenin interacted with 9 amino acids of protective antigen including glutamic acid 117, key factor of anthrax disease, which was -12.3453 *kcal/moll* (Table 3).

***Table 1***

Interaction between propolis compound and protective antigen based on SwissDock

| Ligand name | Receptor | NO. OF SwissDock cluster | Cluster degree | Energy (*kcal/mol*) | Energy ΔG (*kcal/mol*) Of amino acid |
|---|---|---|---|---|---|
| Apigenin | PA | 30 (250 runs) | 1 | -6.22 | -947.67 |
| | | | 2 | -6.02 | -940.61 |
| | | | 3 | -5.99 | -937.55 |
| | | | 4 | -5.81 | -921.54 |
| | | | 5 | -5.80 | -915.39 |
| Rhamnetin | PA | 30 (250 runs) | 1 | -7.06 | -994.80 |
| | | | 2 | -6.46 | -994.77 |
| | | | 3 | -6.35 | -986.33 |
| | | | 4 | -6.21 | -981.24 |
| | | | 5 | -6.20 | -980.23 |
| Tectochrysin | PA | 30 (250 runs) | 1 | -6.59 | -930.25 |
| | | | 2 | -6.58 | -929.84 |
| | | | 3 | -6.45 | -926.36 |
| | | | 4 | -6.37 | -920.28 |
| | | | 5 | -6.31 | -919.27 |
| Pinocembrin | PA | 30 (250 runs) | 1 | -6.82 | -912.43 |
| | | | 2 | -6.74 | -910.60 |
| | | | 3 | -6.73 | -908.14 |
| | | | 4 | -6.62 | -893.87 |
| | | | 5 | -6.60 | -892.39 |

***Table 2***

Interaction between propolis flavonoids and protective antigen by BSP-SLIM server

| Ligand | Docking Score | | | | |
|---|---|---|---|---|---|
| | Score (1) | Score (2) | Score (3) | Score (4) | Score (5) |
| Apigenin | 4.726 | 4.570 | 4.382 | 4.125 | 3.372 |
| Rhamnetin | 5.665 | 4.592 | 4.532 | 4.336 | 4.024 |
| Tectochrysin | 5.271 | 4.275 | 3.724 | 3.463 | 2.817 |
| Pinocembrin | 4.407 | 3.259 | 2.867 | 2.523 | 2.348 |

***Table 3***

Interaction between Propolis flavonoids and protective antigen amino acid

| Ligand | Estimated ΔG (*kcal/mol*) |
|---|---|
| Apigenin | **Asp 148** (-0.3370), **Glu 117** (-12.3453), Gly **116** (-1.3951), **Gly 153** (-0.5462), **Leu 151** (-6.5232), **Ser 52** (-0.4103), **Ser 54** (-3.0104), **Thr 119** (-20.2181), **Va155** (-2.5833). |
| Rhamnetin | **Asn 128**(-3.2204), **Gln 132**(-0.9375), **Glu 122**(-4.0516), **Glu 129**(-4.2142), **lle165**(-1.5798), **Ser 157**(-5.2051). |
| Tectochrysin | **Glu 162** (-5.7558), **His 121** (-7.6844). |
| Pinocembrin | **Asn 128** (-2.4461), **Gln 132** (-0.5863), **His 121** (-6.9734), **Lys 125** (-13.9316), **Lys 161** (-6.8720), **Lys 158** (-8.7244). |

### *Discussion*

This research evidenced that 4 ligands of propolis (Rhamnetin, Apigenin, Tectochrysin, Pinocembrin) had strong interaction with Protective antigen. The results have shown that Apigenin with -12.3453 *kcal/moll*. In accordance with the major role of Protective antigen in anthrax disease and start the mechanism of disease, Apigenin have inhibitory by interfering effect on Protective antigen and its receptor in cell memberance. Apigenin (4′,5,7-trihydroxyflavone), insoluble in water but soluble in organic solvents, a plant flavonoid finding in many plants in the highest amount and predominant flavonoid in pulp (red) of widely in numerous fruits [*Kubola J, Siriamornpun S, 2011*] playing role in defense system against fungal pathogens and insects and also was found [*Lattanzio V et al., 2006*] in propolis [*Narayana K et al., 2001*]. Some studies have assessed pharmaceutical effect and medical benefit of Apigenin healthcare functions in vivo, in vitro such as physiological effect including anti carcinogenesis, ant anti-oxidant [*Ferreira J et al., 2017*], regulates hyperglycaemia (thyroid dysfunction) [*Panda S, Kar A, 2007*], anti-inflammatory [*Lee J et al., 2007*], autoimmune disorders, rheumatoid arthritis [*Ali F et al., 2017*]. Also Zhang and colleague find out the effect of Apigenin in the regulation of cholesterol metabolism and protection of blood vessels by enhancing the activity of superoxide dismutase [*Zhang K et al., 2017*] and Lee and colleague asserts Apigenin anticancer activity by suppressing glucose transporter 1 expression in cultured cancer cells [*Lee Y et al., 2016*] psychological effect such as Parkinson's disease, Alzheimer's disease [*Ali F et al., 2017*], antidepressant properties of apigenin [*Nakazawa T et al., 2003*].Taken together, in the present study, detailed accounts of the properties of inhibitory effect of apigenin and introducing it to be considered as potent therapeutic agent in producing drug to overcome anthrax.

### *Conclusion*

Evidently, the research results attributed that the strongest inhibitory effect of apigenin and the highest Fullfitness of Rhamnetin on protective antigen of anthrax toxin. These results further suggest that apigenin may be effective, as a therapeutic agent in pharmaceutical studies, for therapeutic management of anthrax diseases.

## *REFERENCES*

1. *Ali F, Rahul, Naz F, Jyoti S, Siddique YH (2017)*. Health functionality of apigenin: A review. Int J Food Prop. 20(6): 1197-1238. DOI: 10.1080/10942912.2016.1207188
2. *Blaustein RO, Koehler TM, Collier RJ, Finkelstein A (1989)*. Anthrax toxin: channel-forming activity of protective antigen in planar phospholipid bilayers. Proc Natl Acad Sci U S A. 86(7): 2209-2213. DOI: 10.1073/pnas.86.7.2209

3. *Collier RJ, Young JAT (2003)*. Anthrax toxin. Annu Rev Cell Dev Biol. 19: 45-70. DOI: 10.1146/annurev.cellbio.19.111301.140655
4. *Dar D, Sorek R (2017)*. Regulation of antibiotic-resistance by non-coding RNAs in bacteria. Curr Opin Microbiol. 30(36): 111-117. DOI: 10.1016/j.mib.2017.02.005
5. *Ferreira JM, Fernandes-Silva CC, Salatino A, Negri G, Message D (2017)*. New propolis type from north-east Brazil: chemical composition, antioxidant activity and botanical origin. J Sci Food Agric. 97(11): 3552-2558. DOI: 10.1002/jsfa.8210
6. *Kubola J, Siriamornpun S (2011)*. Phytochemicals and antioxidant activity of different fruit fractions (peel, pulp, aril and seed) of Thai gac (Momordica cochinchinensis Spreng). Food Chem. 127(3): 1138-1145. DOI: 10.1016/j.foodchem.2011.01.115
7. *Lattanzio V, Lattanzio VMT, Cardinali A, Amendola V (2006)*. Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. Phytochemistry. 23-67 ISBN: 81-308-0034-9
8. *Lee JH, Zhou HY, Cho SY, Kim YS, Lee YS., et al (2007)*. Anti-inflammatory mechanisms of apigenin: inhibition of cyclooxygenase-2 expression, adhesion of monocytes to human umbilical vein endothelial cells, and expression of cellular adhesion molecules. Arch Pharm Res. 30(10): 1318-1327. DOI: 10.1007/BF02980273
9. *Lee YM, Lee G, Oh TI, Kim BM, Shim DW., et al (2016)*. Inhibition of glutamine utilization sensitizes lung cancer cells to apigenin-induced apoptosis resulting from metabolic and oxidative stress. Int J Oncol. 48(1): 399-408. DOI: 10.3892/ijo.2015.3243
10. *Milne JC, Furlong D, Hanna PC, Wall JS, Collier RJ (1992)*. Anthrax protective antigen forms oligomers during intoxication of mammalian cells. J Biol Chem. 269(32): 20607-20612. DOI: 10.1016/S0021-9258(17)32036-7
11. *Mohammadi E, Gavanji S, Khozimeh F, Golestannejad Z, Golestannejad M., et al (2017)*. Forecasting of interaction between bee propolis and protective antigenic domain in anthrax using the software and bioinformatics web servers. Tehran Univ Med J. 74(10): 715-722.
12. *Molloy SS, Bresnahan PA, Leppla SH, Klimpel KR, Thomas G (1992)*. Human furin is a calcium-dependent serine endoprotease that recognizes the sequence Arg-X-X-Arg and efficiently cleaves anthrax toxin protective antigen. J Biol Chem. 267(23): 16396-16402. DOI: 10.1016/S0021-9258(18)42016-9
13. *Mushayabasa S, Marijani T, Masocha M (2017)*. Dynamical analysis and control strategies in modeling anthrax. Comput Appl Math. 36(3): 1333-1348
14. *Nakazawa T, Yasuda T, Ueda J, Ohsawa K (2003)*. Antidepressant-like effects of apigenin and 2,4,5-trimethoxycinnamic acid from Perilla frutescens in the forced swimming test. Biol Pharm Bull. 26(4): 474-480. DOI: 10.1248/bpb.26.474
15. *Narayana KR, Reddy MS, Chaluvadi MR, Krishna DR (2001)*. Bioflavonoids Classification, Pharmacological, Biochemical Effects and Therapeutic Potential. Indian J Pharmacol. 33(1): 2-16
16. *Nickell ZD, Moran MD (2017)*. Disease Introduction by Aboriginal Humans in North America and the Pleistocene Extinction. J Ecol Anthropol. 19(1): 29-41
17. *Panda S, Kar A (2007)*. Apigenin (4',5,7-trihydroxyflavone) regulates hyperglycaemia, thyroid dysfunction and lipid peroxidation in alloxan-induced diabetic mice. J Pharm Pharmacol. 59(11): 1543-1548. DOI: 10.1211/jpp.59.11.0012
18. *Pang S, Yee M, Saba Y, Chino T (2018)*. Artepillin C as a targeting survivin molecule in oral squamous cell carcinoma cells in vitro: A preliminary study. J Oral Pathol Med. 47(1): 48-52. DOI: 10.1111/jop.12624
19. *Pearson HE, Iida M, Orbuch RA, McDaniel NK, Nickel KP., et al (2018)*. Overcoming resistance to cetuximab with honokiol, a small-molecule polyphenol. Mol Cancer Ther. 17(1): 204-214. DOI: 10.1158/1535-7163.MCT-17-0384

20. *Saedi Z, Gavanji S, Mohabatkar H (2017)*. Predicting inhibitor of anthrax toxin receptor on human cells using bioinformatics tools. JMBS. 8(1): 70-80

21. *Siamudaala VM, Bwalya JM, Munang'andu HM, Sinyangwe PG, Banda F., et al (2006)*. Ecology and epidemiology of anthrax in cattle and humans in Zambia. Jpn J Vet Res. 54(1): 15-23. DOI: 10.14943/jjvr.54.1.15

22. *Simone-Finstrom M, Borba RS, Wilson M, Spivak M (2017*). Propolis counteracts some threats to honey bee health. Insects. 8(2): 1-20. DOI: 10.3390/insects8020046

23. *Sitali DC, Mumba C, Skjerve E, Mweemba O, Kabonesa C., et al (2017)*. Awareness and attitudes towards anthrax and meat consumption practices among affected communities in Zambia: A mixed methods approach. PLOS Negl Trop Dis. 11(5): e0005580 DOI: 10.1371/journal.pntd.0005580

24. *Tournier J-N, Ulrich RG, Quesnel-Hellmann A, Mohamadzadeh M, Stiles BG (2009)*. Anthrax, toxins and vaccines: a 125-year journey targeting Bacillus anthracis. Expert Rev Anti Infect Ther. 7(2): 219-236. DOI: 10.1586/14787210.7.2.219

25. *Turnbull PCB (2002)*. Introduction: anthrax history, disease and ecology. Curr Top Microbiol Immunol. 271: 1-19. DOI: 10.1007/978-3-662-05767-4_1

26. *Zhang K, Song W, Li D, Jin X (2017)*. Apigenin in the regulation of cholesterol metabolism and protection of blood vessels. Exp Ther Med. 13(5): 1719-1724. DOI: 10.3892/etm.2017.4165

THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023). Issue 4

## CONTENTS

4. *Avagyan S.A., Zilfyan A.V., Muradyan A.A.*
SELECTIVE ADMINISTRATION OF POLYAMINE-DEFICIENT AND POLYAMINE-FREE DIETS TO CANCER PATIENTS

17. *Alshehri K., Morsi N., Mahsoon A.*
THE EFFECT OF WORKPLACE BULLYING ON NURSES' MENTAL WELL-BEING IN SAUDI ARABIA

31. *Saduakas A.Y., Kurakbayev K.K., Matkerimov A.Zh., Tergeussizov A.S., Sagatov I.Y., Shamshiyev A.S., Zhakubayev M.A., Baubekov A.A., Tajibayev T.K., Khanshi Mead, Kozhamkul A.Zh., Madadov I.K.*
THE BENEFITS OF DUPLEX SCANNING OF EXTRACRANIAL CAROTID PATHOLOGIES FOR RISK STRATIFICATION OF ISCHEMIC STROKE

36. *Soleimantabar H., Sabouri S., Shirbandi K.*
RISK OF CARDIAC ANOMALIES IN ABERRANT RIGHT SUBCLAVIAN ARTERY RELATIVE AORTIC ARCH ANOMALIES FOR PEDIATRICS: A CROSS-SECTIONAL STUDY

42. *Abbaspour M., Hejazi Z.S., Namjoyan F., Azemi M.E.*
FORMULATION OF VAGINAL CREAM CONTAINING EXTRACTS OF LINUM USITATISSIMUM, FOENICULUM VULGARE, AND SALVIA OFFICINALIS FOR THE TREATMENT OF ATROPHIC VAGINITIS IN POSTMENOPAUSAL

48. *Zargar M., Najafian M., Shojaei K., Moradkhani N.*
AN INVESTIGATION INTO THE IMPACT OF CONTINUING OR TERMINATING PREGNANCY ON THE MATERNAL, FETAL AND DISEASE PROGRESSION OUTCOMES IN PREGNANT WOMEN WITH COVID-19

58. *Martusevich A.K., Fedotova A.S., Surovegina A.V., Nazarov V.V.*
PLASMA BIOMEDICINE: MODERN STATE-OF-ART AND PERSPECTIVES IN REGENERATIVE MEDICINE

66. *Martusevich A.K., Kovaleva L.K., Fedotova A.S., Stepanova E.A., Soloveva A.G.*
EXPERIMENTAL STUDY OF ERYTHROCYTE ENERGY METABOLISM UNDER INHALATIONS OF NITRIC OXIDE

71. *Bakhtari A., Gavanji S.*
IN-SILICO DOCKING ANALYSIS OF SELECTED FLAVONOIDS AND PROTECTIVE ANTIGEN

77. *Kheradmand P., Shafeenia R., Bagheri S., Attar A.*
CAUDAL TYPE HOMEOBOX 2 EXPRESSION AND PROGNOSTIC FACTORS IN PATIENTS WITH GASTRIC ADENOCARCINOMA

84. *Darmadi D.*
IMPROVEMENT OF ENZYME IMMUNODETECTION IN THE LABORATORY DIAGNOSIS OF HEPATITIS E VIRUS

98. *Tkhruni F.N., Israyelyan A.L., Karapetyan K.J.*, Balabekyan Ts.R., Khachatryan L.M., Khachatryan T.V.*
COMPARATIVE ANTIMICROBIAL ACTIVITY OF SOME METABIOTICS SYNTHESIZED BY LACTIC ACID BACTERIA

110. *Harutyunyan L.*
MODERN APPROACHES TO THE SYSTEMIC TREATMENT OF RECURRENT OVARIAN CANCER

119. *Absoian T., Hameed Alwan M*
ASSOCIATION BETWEEN CAFFEINE, ANXIETY AND THE OCCURRENCE OF APHTHOUS STOMATITIS IN THE ARMENIAN ETHNICITY

# THE NEW ARMENIAN MEDICAL JOURNAL

Volume17 (2023). Issue 4



The Journal is founded by
Yerevan State Medical
University after M. Heratsi.

**Rector of YSMU**

Armen A. Muradyan



**Address for correspondence:**

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

**Phones:**

(+37410) 582532 YSMU
(+37493 588697 Editor-in-Chief
**Fax:** (+37410) 582532
**E-mail:**namj.ysmu@gmail.com, ysmiu@mail.ru
**URL:**http//www.ysmu.am



*Our journal is registered in the databases of Scopus, EBSCO and Thomson Reuters (in the registration process)*

SCOPUS EBSCO
REUTERS

**Copy editor: Tatevik R. Movsisyan**

Printed in "LAS Print" LLC
Director: Suren A. Simonyan
Armenia, 0023,Yerevan,
Acharyan St. 44 Bulding,
Phone: (+374 10) 62 76 12,
E-mail: las.print@yahoo.com