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EDITED BY
Tiţa Ovidiu,
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Mahdi Vajdi,
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Petre Savescu,
University of Craiova, Romania

*CORRESPONDENCE
Angelina Baskovtceva
✉ baskovtseva.ang@yandex.com

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Modeling of lipolysis in the human body and the methodology for developing technology of supplements for obesity prevention considering the utilization of food industry by-products

Vladimir Sadovoy[1,2], Nadezhda Barakova[3,4], Angelina Baskovtceva[3]*, Elena Kiprushkina[3,4], Grigory Tochilnikov[5] and Mark Shamtsyan[4]

[1]Department of Commodity Science and Public Catering Technology, Stavropol Institute of Cooperation (Branch), Belgorod University of Cooperation, Economics, and Law, Stavropol, Russia, [2]Departments of Food Technology and Commodity Science, Institute of Service, Tourism and Design (Branch), North-Caucasian Federal University, Pyatigorsk, Russia, [3]Faculty of Biotechnology, ITMO University, St. Petersburg, Russia, [4]Department of Microbiological Synthesis Technology, St. Petersburg State Technological Institute (Technical University), St. Petersburg, Russia, [5]N.N. Petrov National Research Center of Oncology of the Ministry of Health of Russia, St. Petersburg, Russia

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1 Introduction

Obesity is a serious global problem, and extensive research is being conducted on this topic. Obesity is a risk factor for the development of various diseases such as diabetes, atherosclerosis, hypertension, etc. (1–5). It is known that as body weight decreases, there are processes in the body that counteract weight loss and promote relapse of the disease. Therefore, despite certain successes in obesity treatment, the priority lies in the development of new comprehensive approaches that target the diverse disorders in the energy metabolism system, aiming not only to reduce body weight but also to prevent disease relapse (6–9).

The modern pharmaceutical market offers a wide range of drugs for weight reduction (10, 11). One commonly used drug is based on orlistat, a specific inhibitor of gastrointestinal lipases. This drug exhibits high lipophilicity and interacts with fat globules. Orlistat covalently binds to the active site of pancreatic and gastric lipases, thereby inactivating them. As a result of inhibiting gastrointestinal lipases, triglycerides cannot enter the bloodstream (12, 13). This creates an energy deficit, leading to the mobilization of fat from the depot. The drug is manufactured by many pharmaceutical companies, such as Polpharma (Poland), Izvarino Pharma (Russia), and KRKA (Slovenia). The most popular supplements for weight loss include conjugated linoleic acid (CLA) and L-carnitine (14, 15).

CLA's mechanism of action involves influencing the lipase enzyme function. This nutrient helps prevent the accumulation of excess adipocyte cells in subcutaneous adipose tissue and accelerates the process of lipolysis (the metabolic process of fat splitting) (16). On the other hand, L-carnitine acts as a carrier for fats, speeding up their metabolism. It does not

participate in the fat-splitting reaction or any other reactions. After the fat molecule is split apart inside the cell, the drug is excreted with its structure virtually unchanged. During the breakdown of fat cells, a significant amount of energy, water, and carbon dioxide is released. In other words, it facilitates a natural metabolic process that the drug accelerates (17–20).

2 Methods of pancreatic lipase inhibition

2.1 The use of computational chemistry and artificial intelligence in modeling and optimizing the lipolysis process

The utilization of computational chemistry and artificial intelligence aims to minimize the need for costly experimentation. It is crucial to accurately perform geometric optimization of the studied dietary supplements and investigate their molecular properties, including dipole moment, RMS gradient, electron density, and potential energy. Analyzing the changes in potential energy, atomic charges, synchronous transition state search, and studying the quantum-chemical characteristics of the lipase ligand will provide insights into the variations in the activity of pancreatic lipase in the presence of different dietary supplements. For this purpose, molecular docking applications are employed (21, 22).

Artificial intelligence (AI) is associated with fuzzy logic methods and proves effective in processing experimental results. Using AI, optimal composition variants can be identified based on multiple parameters when inhibiting pancreatic lipase (23).

2.2 Inhibition of fat accumulation by pancreatic lipase enzyme

Scientists from the Department of Pharmacognosy, JSS College of Pharmacy, India, are engaged in similar studies. Their research suggests that inhibiting fat accumulation through pancreatic lipase enzyme inhibition is an interesting approach in the development of new and safer anti-obesity medications. The pancreatic lipase enzyme is naturally lipolytic and is released from the acinar cells of the pancreas, which play a key role in the breakdown of triglycerides. Thus, the pancreatic lipase enzyme plays an important role in the intestine and is not directly absorbed into the bloodstream, thereby avoiding other associated side effects and complications (24, 25).

2.3 Flavonoids—inhibitors of the pancreatic lipase enzyme

A significant study conducted by researchers from the University of Applied Sciences Upper Austria focused on analyzing various data on bioactive compounds for lipid metabolism regulation. The study highlighted flavonoids such as quercitrin, isoquercitrin, and afzelin, which were found to reduce triglyceride levels and regulate several adipogenic transcription factors, resulting in a decrease in the expression of proteins associated with lipogenesis. The effects of the flavonoid kaempferol and the flavone hesperidin against obesity were described. The research was conducted on 3T3-L1 mouse cells. Kaempferol not only suppressed adipogenesis in preadipocytes by 62% but also reduced intracellular lipid accumulation in mature adipocytes by 39%, while hesperidin was able to reduce intracellular lipids by 88.1% (26, 27).

Phenolic compounds, such as flavonoids, saponins, alkaloids, and terpenoids, may possess inhibitory effects on the pancreatic lipase enzyme. This information is supported by *in silico* computer modeling, which identifies the interactions between phytochemicals and the specific active binding site of the pancreatic lipase enzyme. The inhibitory action of lipase is mainly influenced by two factors: the molecule's size and the positioning of hydroxyl groups (28–30).

2.4 Phenacyl esters of N-phthaloyl amino acids—inhibitors of pancreatic lipase

Veintramuthu Sankara et al., researchers from the Department of Pharmaceutics, PSG College of Pharmacy, India, are investigating the synthesis and biological evaluation of phenacyl esters of N-phthaloyl amino acids as inhibitors of pancreatic lipase using molecular docking. Their *in vitro* and in silico studies have shown the effectiveness of these compounds in inhibiting pancreatic lipase. In silico ADME (absorption, distribution, metabolism, and excretion) studies have suggested that these compounds may possess medicinal properties (31).

2.5 Glutathione disulfide and silibinin (A)—inhibitors of pancreatic lipase

A study conducted by a team of scientists from the Department of Applied Physics, University of Granada (UGR), Spain, has identified new natural compounds from milk thistle components that can inhibit pancreatic lipase. The researchers used the DrugBank database for docking calculations, and the most relevant compounds were further evaluated *in vitro*. The data revealed that glutathione disulfide and silibinin (A) inhibit pancreatic lipase. Therefore, these substances can also serve as promising natural compounds in the fight against obesity (32, 33).

2.6 Protein hydrolysates—inhibitors of pancreatic lipase

Chinese scientists from the School of Food Science and Engineering, South China University, China, have also conducted important research and identified economically efficient natural lipase inhibitors against obesity. This study demonstrated, for the first time, the production of porcine pancreatic lipase inhibitory peptides from inexpensive sea buckthorn seed flour using response surface methodology. The results reflected the optimal conditions for obtaining the protein hydrolysate from sea buckthorn seeds (pH, temperature, enzyme dosage, etc.). Under

these conditions, the protein hydrolysate inhibited lipase activity by approximately 35%. Analysis using LC-MS/MS revealed the presence of 22 arginine-containing peptides in the hydrolysate, six of which were predicted using molecular docking as potential anti-obesity peptides. The inhibitory action of these peptides against pancreatic lipase involved hydrophilic and hydrophobic interactions, hydrogen bonding, and van der Waals interactions (34).

2.7 Plant-based substances facilitating weight loss

Studies describing the positive dyslipidemic effect of ginseng seed oil have attracted great interest. Ginseng, with its high level of ginsenosides as bioactive compounds, reduced lipid content *in vitro* in HepG2 cells and rat hepatocytes, as well as *in vivo* in mice fed a high-fat diet (35, 36).

Another plant, the Indian gooseberry (*Phyllanthus emblica L.*), has a beneficial impact on adipogenesis, as reported by Balusamy et al. from the Department of Food Science and Biotechnology, Sejong University. The researchers found a significant reduction in triglyceride accumulation through the suppression of adiponectin-related adipocyte markers (37).

3 Discussion

Of particular interest are studies conducted by scientists engaged in discovering compounds that inhibit pancreatic lipase using molecular docking methods. One promising direction is the development of technologies for obtaining preventive biologically active substances from by-products. Unfortunately, at present, this source of raw materials is not fully utilized, despite being low-cost or even cost-free and having a chemical composition comparable to the primary raw materials.

By-products from the winemaking industry, such as grape seeds and grape pomace (37), or by-products of corn processing, such as husks, cobs, and vegetative parts (38), can be effectively used for extracting flavonoids. Flavonoids are the most valuable components in grape pomace. According to various literature sources, the content of flavonoids in grape pomace ranges from 0.15 to 0.88% (39, 40).

Allicin is a compound with low thermal stability. It slowly degrades at room temperature and rapidly during heating processes (41, 42). Therefore, it is necessary to develop a technology that ensures the delivery of allicin to the small intestine in its native state. The compound allicin can be obtained from garlic which is classified as waste and doesn't meet the standard requirements.

Lecithin is essential for the formation of intercellular spaces, and it is a component of cell membranes. As a building material, lecithin participates in the regeneration of damaged cells. There is evidence that dietary intake of lecithin reduces the absorption of lipids in the body. The mechanism of action of lecithin involves its influence on the activity of the lipase enzyme, helping to prevent the excessive accumulation of adipocytes in subcutaneous adipose tissue and slowing down the process of lipolysis (the metabolic process of fat splitting) (43, 44). To obtain lecithin, it is suggested to use waste from soy protein concentrate production—soy micelles or soy molasses.

L-carnitine is a naturally occurring substance that is similar to B-group vitamins. It is synthesized in the human body and is present in the liver and muscle fibers. L-carnitine mobilizes fat deposits in tissues by transporting fatty acids across the cell membrane, allowing them to be burned in the mitochondria to produce ATP (adenosine triphosphate) (45, 46).

The main representatives of polyunsaturated fatty acids are omega-3 (docosahexaenoic acid, alpha-linolenic acid, eicosapentaenoic acid) and omega-6 (arachidonic acid, linoleic acid). Polyunsaturated fats improve the rheological properties of blood, reduce the level of cholesterol deposits on blood vessel walls, protect cellular membrane lipids from oxidation, and lower triglyceride levels (47, 48). New technologies are being developed to produce omega-3 and omega-6 from by-products of the fish industry, which will help reduce the cost of the final products (49).

The studies involving *in vivo* analysis of the lipolysis process and its regulation using computational chemistry techniques are of particular importance (50).

It is of current interest to investigate the mechanism of lipolysis by studying the intermolecular interactions between the biologically active components of dietary supplements and pancreatic lipase and also to develop compositions that promote activation of metabolic processes, reduction of lipolysis, and decreased fat absorption.

The analysis of the lipolysis mechanism is conducted using computational chemistry methods, which involve the modeling of spatial structures of biologically active substances. Geometric optimization, quantum-chemical characteristics, and charge density distribution of the investigated food supplements and pancreatic lipase molecules enable the prediction of the chemical composition of ingredients that contribute to the reduction of fat absorption in the body. The molecular properties of human pancreatic lipase before and after molecular docking can be studied to determine the conditions for complete blockage of the enzyme's active site.

In addition to studying lipolysis, it is possible to develop preparations that activate metabolism, reduce fat absorption in the intestine, and so on. To scientifically justify the compositional formulation and develop the technology of biologically active supplements for the prevention of obesity, it is necessary to employ semi-empirical methods and molecular mechanics techniques. Based on the conducted experimental research, with the aid of statistical neural networks, it is important to scientifically substantiate and develop compositions of food supplements with preventive properties. The obtained compositions should be evaluated using laboratory animals for their qualitative characteristics, biological value, preventive properties, safety, and harmlessness. Based on the results of these studies, recommendations for their use in nutrition should be developed (51).

One of the means to combat obesity is the inhibition of lipase by biologically active substances of plant and animal origin, extracted, including from secondary raw materials. The evaluation of substance action on lipase is recommended to

be conducted through the modeling of spatial structures of biologically active substances using computer chemistry methods and determining the quantum-chemical characteristics and charge density of the molecules of the investigated biologically active substances and lipase.

The use of computer chemistry and artificial intelligence will minimize the costly experiment. It is crucial to accurately perform the geometric optimization of the investigated BADs and examine their molecular properties (dipole moment, RMS gradient, electron density, potential energy).

Author contributions

VS: Investigation, Writing – review & editing. NB: Conceptualization, Investigation, Writing – original draft. AB: Investigation, Writing – original draft. EK: Conceptualization, Writing – review & editing. GT: Conceptualization, Investigation, Writing – original draft. MS: Conceptualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Li G, Wang Q, Chen X, Yu P, Peng Q, Chen H, et al. Based on network pharmacology to explore the effect and mechanism of Yipibushen decoction in improving obese type 2 diabetes mellitus with oligoasthenotspermia. *J Ethnopharmacol.* (2023) 317:116738. doi: 10.1016/j.jep.2023.116738

2. Song X, Wang C, Wang T, Zhang S, Qin J. Obesity and risk of gestational diabetes mellitus: a two-sample Mendelian randomization study. *Diabetes Res Clin Pract.* (2021) 197:110561. doi: 10.1016/j.diabres.2023.110561

3. Sohrabi Y, Reinecke H. RIPK1 targeting protects against obesity and atherosclerosis. *Trends Endocrinol Metabol.* (2021) 32:420–2. doi: 10.1016/j.tem.2021.03.009

4. Ahn SJ, Le Master E, Granados ST, Levitan I. Chapter One – Impairment of endothelial glycocalyx in atherosclerosis and obesity. *Curr Top Membr.* (2023) 91:1–19. doi: 10.1016/bs.ctm.2023.02.001

5. Bloodworth M, Shuey M, Staso P, Huang S, Wells Q, Cahill K. Risk factors for asthma development in adult patients in the electronic health record: a landmark analysis from the Vanderbilt CardiOvascular and Multiple MetabOlic Disease in Obesity Resource (COMMODORE). *J Aller Clin Immunol.* (2023) 151:AB115. doi: 10.1016/j.jaci.2022.12.366

6. Wahab RA, Le Roux CW. A review of the evidence on cardiovascular outcomes from obesity treatment. *Obesity Pillars.* (2023) 7:100071. doi: 10.1016/j.obpill.2023.100071

7. Davisson L, Hernandez MA, Haggerty TS. Primary care treatment of obesity in West Virginia: a needs assessment. *Obes Med.* (2022) 34:100445. doi: 10.1016/j.obmed.2022.100445

8. MacCannell AD, Roberts LD. Metabokines in the regulation of systemic energy metabolism. *Curr Opin Pharmacol.* (2022) 67:102286. doi: 10.1016/j.coph.2022.102286

9. Stylianopoulou C. Carbohydrates: regulation of metabolism. *Encycl Hum Nutr.* (2023) 126–35. doi: 10.1016/B978-0-12-821848-8.00173-6

10. Ribeiro Pinto Bravo T, Mendes Luquetti T, Amorim Nogueira T, Calil-Elias S. Quality of information on weight loss drugs from South American websites. *Obesity Medicine.* (2022) 33:100438. doi: 10.1016/j.obmed.2022.100438

11. Lazzaroni E, Ben Nasr M, Loretelli C. Anti-diabetic drugs and weight loss in patients with type 2 diabetes. *Pharmacol Res.* (2021) 171:105782. doi: 10.1016/j.phrs.2021.105782

12. Braeckmans M, Brouwers J, Mols R, Servais C. Orlistat disposition in the human jejunum and the effect of lipolysis inhibition on bile salt concentrations and composition. *Int J Pharm.* (2022) 621:121807. doi: 10.1016/j.ijpharm.2022.121807

13. Mandal SK, Kumar BK, Sharma PK, Murugesan S, Deepa PR. *In silico* and *in vitro* analysis of PPAR – α/γ dual agonists: comparative evaluation of potential phytochemicals with anti-obesity drug orlistat. *Comput Biol Med.* (2022) 147:105796. doi: 10.1016/j.compbiomed.2022.105796

14. Badawy S, Liu Y, Guo M, Liu Z, Xie C, Marawan MA, et al. Conjugated linoleic acid (CLA) as a functional food: is it beneficial or not? *Food Res Int.* (2023) 172:113158. doi: 10.1016/j.foodres.2023.113158

15. Su C, Chang C, Chou C. L-carnitine ameliorates dyslipidemic and hepatic disorders induced by a high-fat diet via regulating lipid metabolism, self-antioxidant capacity, and inflammatory response. *J Funct Foods.* (2015) 15:497–508. doi: 10.1016/j.jff.2015.04.007

16. Haghighat N, Shimi G, Shiraseb F, Karbasi A, Nadery M, Ashtary-Larky D, et al. The effects of conjugated linoleic acid supplementation on liver function enzymes and malondialdehyde in adults: a GRADE-assessed systematic review and dose-response meta-analysis. *Pharmacol Res.* (2022) 186:106518. doi: 10.1016/j.phrs.2022.106518

17. Chizmichyan EE, Andreeva IN. Analysis of consumer preferences for weight loss medications and dietary supplements. *Izvestiya High Educ Inst N Caucasus Reg. Series Nat Sci.* (2006) 523:18–19. Available online at: https://cyberleninka.ru/article/n/analiz-potrebitelskih-predpochteniy-lekarstvennyh-sredstv-i-bad-k-pische-dlya-snizheniya-massy-tela/viewer

18. Sandner G, König A, Wallner M, Weghuber J. Functional foods - dietary or herbal products on obesity: application of selected bioactive compounds to target lipid metabolism. *Current Opin Food Sci.* (2020) 34:9–20. doi: 10.1016/j.cofs.2020.09.011

19. Sawicka B, Krochmal-Marczak B, Skiba D, Bienia B. Chapter 9 – Herbal carbohydrates in healthcare. *Herb Biomol Healthcare Appl.* (2022) 2022:185–204. doi: 10.1016/B978-0-323-85852-6.00027-5

20. Romm A, Ganora L, Hoffmann D. CHAPTER 3 – fundamental principles of herbal medicine. *Bot Med Women's Health.* (2010) 24–74. doi: 10.1016/B978-0-443-07277-2.00003-9

21. Gertig C, Leonhard K, Bardow A. Computer-aided molecular and processes design based on quantum chemistry: current status and future prospects. *Curr Opin Chem Eng.* (2020) 27:89–97. doi: 10.1016/j.coche.2019.11.007

22. Capitan-Vallvey LF, Lopez-Ruiz N, Martinez-Olmos A, Erenas MM, Palma AJ. Recent developments in computer vision-based analytical chemistry: a tutorial review. *Anal Chim Acta.* (2015) 899:23–56. doi: 10.1016/j.aca.2015.10.009

23. Espinosa Sandoval LA, Polania Rivera AM, Castaneda Florez L. Chapter 13 – Application of artificial neural networks (ANN) for predicting the effect of processing on the digestibility of foods. *Food Struct Eng Design Impr Nut Health Well-Being.* (2023) 333–61. doi: 10.1016/B978-0-323-85513-6.00011-6

24. Li R, Xue Z, Jia Y, Wang Y. Polysaccharides from mulberry (*Morus alba* L) leaf prevents obesity by inhibiting pancreatic lipase in high-fat diet induced mice. *Int J Biol Macromol.* (2021) 192:452–60. doi: 10.1016/j.ijbiomac.2021.10.010

25. Nayebhashemi M, Enayati S, Zahmatkesh M, Madanchi H, Saberi S, Mostafavi E, et al. Surface display of pancreatic lipase inhibitor peptides by engineered Saccharomyces boulardii: Potential as an anti-obesity probiotic. *J Funct Foods.* (2023) 102:105458. doi: 10.1016/j.jff.2023.105458

26. Sadovoy VV, Shchedrina TV, Selimov MA, Nagdalian AA. Nutritional supplement for control of diabetes. *J Excip Food Chem.* (2017) 2:31–8. Available online at: https://www.researchgate.net/publication/321309622_Nutritional_supplement_for_control_of_diabetes

27. Li M, Chen Y, Ruan J, Wang W, Chen J, Zhang Q. Structure-activity relationship of dietary flavonoids on pancreatic lipase. *Current Res Food Sci.* (2023) 6:100424. doi: 10.1016/j.crfs.2022.100424

28. Sankar V, Engels SEM. Synthesis, biological evaluation, molecular docking and in silico ADME studies of phenacyl esters of N-Phthaloyl amino acids as pancreatic lipase inhibitors. *Fut J Pharm Sci.* (2018) 4:276–83. doi: 10.1016/j.fjps.2018.10.004

29. Cercato LM, Oliveira JP, Santana Souza MT, Andrade N, Martel F, Camargo EA. Effect of flavonoids in preclinical models of experimental obesity. *PharmaNutrition.* (2021) 16:100260. doi: 10.1016/j.phanu.2021.100260

30. Hao Y, Zhou F, Dong J, Wang Y, Lang Z, Li S, et al. Study on the role of flavonoids derived extract from seed residues of hippophae rhamnoides on high-fat diet induced obese mice. *J King Saud Univ Sci.* (2019) 32:1597–603. doi: 10.1016/j.jksus.2019.12.017

31. Xiang H, Waterhouse D, Liu P, Waterhouse GIN Li J, Cui C. Pancreatic lipase-inhibiting protein hydrolysate and peptides from seabuckthorn seed meal: preparation optimization and inhibitory mechanism. *LWT.* (2020) 134:109870. doi: 10.1016/j.lwt.2020.109870

32. Castillo-Santaella TD, Hernandez-Morante JJ, Suarez-Olmos J, Maldonado-Valderrama J, Pena-Garcia J, Cortes CM, et al. Identification of the thistle milk component Silibinin(A) and Glutathione-disulphide as potential inhibitors of the pancreatic lipase: Potential implications on weight loss. *J Funct Foods.* (2021) 83:104479. doi: 10.1016/j.jff.2021.104479

33. Tang Y, Zhan W, Li M, Wang L, Wei J, Deng J, et al. Glutathione inhibited starch digestion: Structural and kinetic analysis of substrate and α-amylase. *Food Chem.* (2023) 405:134979. doi: 10.1016/j.foodchem.2022.134979

34. Karoud W, Brahmi N, Hamed H, Allagui M, Bougatef A, Sila A. Hake heads proteins hydrolysates as a source of bioactive peptides with prevention against hypercholesterolemia in mice: the involvement of oxidative dysfunction in hepatic tissues. *Food Chem Adv.* (2023) 2:100266. doi: 10.1016/j.focha.2023.100266

35. Min JE, Long NP, Hong JY, Kim SJ, Nguyen AH, Wang D, et al. The dehiscence process in Panax ginseng seeds and the stigmasterol biosynthesis pathway in terms of metabolomics. *J Ginseng Res.* (2022) 46:225–34. doi: 10.1016/j.jgr.2021.06.005

36. Kim GW, Jo HK, Chung SH. Ginseng seed oil ameliorates hepatic lipid accumulation *in vitro* and *in vivo*. *J Ginseng Res.* (2018) 42:419–28. doi: 10.1016/j.jgr.2017.04.010

37. Balusamy SR, Veerappan K, Ranjan A, Kim Y-J, Chellappan DK, Dua K, et al. Phyllanthus emblica fruit extract attenuates lipid metabolism in 3T3-L1 adipocytes via activating apoptosis mediated cell death. *Phytomedicine.* (2020) 66:153129. doi: 10.1016/j.phymed.2019.153129

38. Sirohi R, Tarafdar A, Singh S, Negi T, Gaur VK, Gnansounou E, et al. Green processing and biotechnological potential of grape pomace: current trends and opportunities for sustainable biorefinery. *Bioresour Technol.* (2020) 314:123771. doi: 10.1016/j.biortech.2020.123771

39. Cui W, Wang Y, Sun Z, Cui C, Li H, Luo K, et al. Effects of steam explosion on phenolic compounds and dietary fiber of grape pomace. *LWT.* (2023) 173:114350. doi: 10.1016/j.lwt.2022.114350

40. Abouelenein D, Mustafa AM, Caprioli G, Ricciutelli M, Sagratini G, Vittori S. Phenolic and nutritional profiles, and antioxidant activity of grape pomaces and seeds from Lacrima di Morro d'Alba and Verdicchio varieties. *Food Biosci.* (2023) 53:102808. doi: 10.1016/j.fbio.2023.102808

41. Gruhlke MCH, Antelmann H, Bernhardt J, Kloubert V, Rink L, Slusarenko AJ. The human allicin-proteome: S-thioallylation of proteins by the garlic defence substance allicin and its biological effects. *Free Radic Biol Med.* (2019) 131:144–53. doi: 10.1016/j.freeradbiomed.2018.11.022

42. Cui T, Liu W, Chen S, Yu C, Li Y, Zhang J-Y. Antihypertensive effects of allicin on spontaneously hypertensive rats via vasorelaxation and hydrogen sulfide mechanisms. *Biomed Pharmacother.* (2020) 128:110240. doi: 10.1016/j.biopha.2020.110240

43. Ng DS. Lecithin cholesterol acyltransferase deficiency protects from diet-induced insulin resistance and obesity – novel insights from mouse models. *Vit Horm.* (2013) 91:259–70. doi: 10.1016/B978-0-12-407766-9.00011-0

44. Sadovoy VV, Shchedrina TV, Selimov MA. Biologically active composition for regulation of lipolysis process in the organism under obesity. *Vopr Pitan.* (2017) 86:74–83. Available online at: https://www.researchgate.net/publication/324528028_Biologically_active_composition_for_regulation_of_lipolysis_process_in_the_organism_under_obesity

45. Zachariah JP, Pena S, Lupo PJ, Putluri N, Penny DJ, Richard MA. Effect of exogenous l-carnitine on aortic stiffness in dyslipidemic adolescents: design of a quadruple-blind, randomized, controlled interventional trial. *Contemp Clin Trials Commun.* (2023) 34:101174. doi: 10.1016/j.conctc.2023.101174

46. Alhasaniah AH. L-carnitine: Nutrition, pathology, and health benefits. *Saudi J Biol Sci.* (2023) 30:103555. doi: 10.1016/j.sjbs.2022.103555

47. Soma PS, Ehrmann BM. Dataset linking free polyunsaturated fatty acid concentrations in erythrocytes with chronic pain conditions in adults. *Data Brief.* (2023) 46:108802. doi: 10.1016/j.dib.2022.108802

48. Wang J, Yu X, Wang K, Lin L, Liu H-H, Ledesma-Amaro R, et al. Reprogramming the fatty acid metabolism of *Yarrowia lipolytica* to produce the customized omega-6 polyunsaturated fatty acids. *Bioresour Technol.* (2023) 383:129231. doi: 10.1016/j.biortech.2023.129231

49. Zemlyakova ES, Mezenova OY. *Biologically Active Compositions With Osteotropic and Chondroprotective Effects Based on Secondary Raw Materials of Hydrobionts*. Kaliningrad: FGOU VPO "KGTU" (2011). p. 120–69.

50. Schulze MB, Minihane AM, Saleh RNM, Risérus U. Intake and metabolism of omega-3 and omega-6 polyunsaturated fatty acids: nutritional implications for cardiometabolic diseases. *Lancet Diab Endocrinol.* (2020) 8:915–30. doi: 10.1016/S2213-8587(20)30148-0

51. Azad U, Singh H. Quantum chemistry calculations using energy derivatives on quantum computers. *Chem Phys.* (2022) 558:111506. doi: 10.1016/j.chemphys.2022.111506