DOI: 10.20514/2226-6704-2026-16-2-104-112
УДК [616.34-008.8:616.-008.9-06:616.12]-07-085
EDN: LXOECG

Е.В. Резник[1,2,3], Л.Х. Алиева[1,3], В.А. Фефелова[1], Л.И. Кафарская[1]

[1] — ФГАОУ ВО «РНИМУ им. Н.И. Пирогова» Минздрава РФ, Москва, Россия
[2] — ГБУЗ «ГКБ № 31» им. Г.М. Савельевой ДЗМ, Москва, Россия
[3] — ГБУЗ «ГКБ № 67» им. Л.А. Ворохобова ДЗМ», Москва, Россия

ГИПЕРУРИКЕМИЯ И СЕРДЕЧНО-СОСУДИСТЫЙ РИСК: МИКРОБИОТА КИШЕЧНИКА — КЛЮЧЕВОЕ ЗВЕНО ПАТОГЕНЕЗА И НОВАЯ МИШЕНЬ ТЕРАПИИ

E.V. Reznik[1,2,3], L.Kh. Alieva[1,3], V.A. Fefelova[1], L.I. Kafarskaya[1]

[1] — Federal State Autonomous Educational Institution of Higher Education «Russian National Research Medical University named after N.I. Pirogov» Ministry of Health of the Russian Federation, Moscow, Russia
[2] — G.M. Savelieva City Clinical Hospital No. 31, Moscow, Russia
[3] — L.A. Vorokhobov City Clinical Hospital No. 67, Moscow, Russia

Hyperuricemia and cardiovascular risk: gut microbiota as a key link in pathogenesis and a new target for therapy

Резюме

Гиперурикемия — это значимый и самостоятельный фактор риска сердечно-сосудистых заболеваний. В последние годы внимание ученых привлекает микробиота кишечника и ее влияние на различные процессы в организме человека. На данный момент существуют доказательства важной роли микробиоты в патогенезе гиперурикемии. Увеличение численности патогенной микрофлоры способствует вялотекущему воспалению и повышению уровня мочевой кислоты через механизмы метаболизма пуринов. Цель данного обзора заключается в анализе и систематизации современных данных о влиянии кишечной микробиоты в патогенезе гиперурикемии и сердечно-сосудистого риска. В статье обсуждаются перспективные методы коррекции гиперурикемии, такие как модификация образа жизни, трансплантация фекальной микробиоты, пробиотики и постбиотики. Обзор подчёркивает необходимость дальнейшего изучения микробиоты как ключевого звена патогенеза гиперурикемии и разработки новых, инновационных терапевтических стратегий.

Ключевые слова: *гиперурикемия; сердечно-сосудистые заболевания; микробиота кишечника; пробиотики; постбиотики*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Статья получена 10.08.2025 г.
Одобрена рецензентом 15.09.2025 г.
Принята к публикации 10.10.2025 г.

Для цитирования: Резник Е.В., Алиева Л.Х., Фефелова В.А. и др. ГИПЕРУРИКЕМИЯ И СЕРДЕЧНО-СОСУДИСТЫЙ РИСК: МИКРОБИОТА КИШЕЧНИКА — КЛЮЧЕВОЕ ЗВЕНО ПАТОГЕНЕЗА И НОВАЯ МИШЕНЬ ТЕРАПИИ. Архивъ внутренней медицины. 2026; 16(2): 104-112. DOI: 10.20514/2226-6704-2026-16-2-104-112. EDN: LXOECG

Abstract

Hyperuricemia is a significant and independent risk factor for cardiovascular diseases. In recent years, scientists have been paying attention to the gut microbiota and its impact on various processes in the human body. Currently, there is evidence of the important role of the microbiota in the pathogenesis of hyperuricemia. An increase in the number of pathogenic microflora contributes to chronic inflammation and an increase in uric

acid levels through the mechanisms of purine metabolism. The purpose of this review is to analyze and systematize current data on the impact of the intestinal microbiota on the pathogenesis of hyperuricemia and cardiovascular risk. The article discusses promising methods for correcting hyperuricemia, such as lifestyle modification, fecal microbiota transplantation, probiotics, and postbiotics. The review highlights the need for further research on the microbiota as a key factor in the pathogenesis of hyperuricemia and the development of new and innovative therapeutic strategies.

Key words: *hyperuricemia; cardiovascular diseases; gut microbiota; uric acid; probiotics; postbiotics*

Conflict of interests
The authors declare no conflict of interests

Sources of funding
The authors declare no funding for this study

Article received on 10.08.2025
Reviewer approved 15.09.2025
Accepted for publication on 10.10.2025

For citation: Reznik E.V., Alieva L.Kh., Fefelova V.A. et al. Hyperuricemia and cardiovascular risk: gut microbiota as a key link in pathogenesis and a new target for therapy. The Russian Archives of Internal Medicine. 2026; 16(2): 104-112. DOI: 10.20514/2226-6704-2026-16-2-104-112. EDN: LXOECG

HU — hyperuricemia, UA — uric acid, NO — nitrogen oxide, EH — essential hypertension, CVD — cardiovascular disease, SCFA — short-chain fatty acids, BP — blood pressure, XDH — xanthine dehydrogenase, LPS — lipopolysaccharides, L. — Lactobacillus, XO — xanthine oxidase, E — Escherichia, TMAO — trimethylamine N-oxide, FMT — fecal microbiome transplant.

Introduction

Hyperuricemia (HU) presumes the elevation of serum uric acid (UA) levels over 420 μmol/L [1, 2]. In different documents reference UA ranges vary based on the gender, with HU confirmed when UA levels reach ≥ 416.0 μmol/L (7.0 mg/dL) in males or ≥ 357.0 μmol/L (6.0 mg/dL) in females [3]. Asymptomatic HU can be additionally defined as elevated UA levels over 405 μmol/L without clinical manifestations [4].

UA is mainly synthesized in the liver, bowel, and the vascular endothelium as a final metabolic product of exogenous purines (consumed with food) and endogenous purines (formed in damaged, dying, or dead cells) [2, 5, 6].

While extracellular UA acts as an antioxidant, intracellular UA is actually a prooxidant, causing inflammation in endothelial and smooth muscle cells, as well as intracellular oxidative stress, thus leading to endothelial dysfunction [3, 6, 7]. UA affects the renin-angiotensin-aldosterone system via two mechanisms, including the stimulation of renin plasma activity and renal renin expression. Besides, UA was detected in atherosclerotic plaques [3]. It reacts with nitrogen oxide (NO), a very important vasodilator, forming 6-aminouracil and thus depleting NO levels, promoting essential hypertension (EH). UA also prevents NO production by inhibiting endothelial NO synthase and decreases arginine availability, which promotes endothelial dysfunction and EH even more [3, 8]. The PAMELA study has demonstrated that each serum UA level elevation by 1 mg/dL is associated with an approximately 30 % increase in EH risk [8]. It has been confirmed that asymptomatic HU increases the risk of both ischemic and hemorrhagic stroke twice within three years, i.e. asymptomatic HU may be one of the risk factors for strokes and other cardiovascular diseases (CVDs) or complications [7]. UA monitoring is required to support the metabolic health in the population.

Intestinal microbiome specifically contributes to HU. 80 % UA is formed due to the degradation of endogenous purines, while 20 % UA is formed from exogenous purines (i.e. food). A high-purine diet (seafood, animal by-products, alcohol) is a risk factor for HU and an important cause of intestinal microbiome imbalance in patients [3, 9, 10, 11]. Purine nucleotides are hydrolyzed to adenine and guanine, deaminated with the formation of xanthine, and then oxidized to UA [9].

The goal of literature review was to systematize the information about the effects of dysbiosis as an independent CVD risk factor in HU, mediating inflammation and endothelial dysfunction. Studies of microbiome effects on the human health have been active lately, with strategies being developed to affect the microbial composition to treat diseases and achieve active longevity. A microbiome is not a simple concomitant factor, but rather a specific pathogenetic event, acting via purine metabolism mechanisms, neurotransmitter production, stimulation of proinflammatory cytokines, etc. This article discusses the prospective methods of HU correction, including postbiotics, fecal microbiome transplant, and nutrition.

Materials and Methods

The PubMed database was searched for publications devoted to the association of hyperuricemia and cardiovascular diseases, microbiome effects on these conditions published within the prior 5 years (since 2020) using the following search terms: “hyperuricemia and

cardiovascular diseases", "microbiome and hyperuricemia", "microbiome and cardiovascular diseases". A total of 5,397 scientific publications were detected, with 42 (including 5 Russian) articles corresponding to this review topic included into the review.

Results and Discussion

High-performance methods and analytical tools developed within the latest 15 years in the sphere of microbiome studies have changed our views on its importance for the host body. Intestinal microbiome is a complex ecological system, a multicellular metabolically active "organ" consisting of prokaryotic cells, eukaryotic host cells, and bacteriophages, creating a unique intestinal ecosystem.

A sufficient number of studies elucidating the association of HU, CVDs, and intestinal microbiome is currently available. These describe the microbiome effects on UA levels, endothelial dysfunction, participation in atherogenesis; favorable and pathogenic/opportunistic flora has been defined, with alternative treatment methods proposes for different diseases (Table 1).

Compared to patients with normouricemia, patients with HU demonstrated altered microbiome composition characterized by the decreased Coprococcus spp. counts [11]. Coprococcus spp. form the main genera of the Lachnospiraceae Bacillota family which maintain microbial homeostasis and metabolic health, as they promote the production of an important metabolite butyrate [12]. Butyrate is a short-chain fatty acid (SCFD) which plays a key role in maintaining the intestinal health, supplying the colonic cells, improving the barrier function, suppressing inflammation and promoting a balanced microbiome [13]. It also decreases the blood pressure (BP), suppresses the production of proinflammatory cytokines (i.e. tumor necrosis factor α, interleukin 12, interferon γ), and enhances the production of an anti-inflammatory interleukin 10 by monocytes [14], while also suppressing xanthine dehydrogenase (XDH) activity [15]. Thus, decreased Coprococcus counts in patients with HU lead to elevated UA levels, intestinal barrier function worsening, promoting the low-grade inflammation in the body and worsening the CVD prognosis.

The intestinal microbiome in patients with gout was characterized by decreased Faecalibacterium prausnitzii counts [9].

Faecalibacterium prausnitzii is another microbe producing butyrate. Higher microbial counts were reported in patients with normal UA levels [11, 16]. Fecal microbiome sequencing has demonstrated that people with higher Faecalibacterium prausnitzii counts had lower coronary artery disease incidence vs. the control group. In murine studies Faecalibacterium prausnitzii suppressed inflammation and had antiatherosclerotic effects after the oral administration. This effect was caused by the decreased lipopolysaccharide (LPS) synthesis in the bowel along with enhanced mechanical and mucous barriers, thus leading to decreased plasma LPS levels and antiatherosclerotic effects [17].

Collinsella aerofaciens is represented in the colon of a healthy human, producing the formic and lactic acids.

Collinsella spp. modulate serum UA levels via four mechanisms. Firstly, Collinsella spp. directly produce UA. Secondly, Collinsella spp. indirectly inhibit UA degradation by other bacteria. Thirdly, metabolites produced by Collinsella spp. decrease the renal and intestinal UA excretion. Finally, Collinsella spp. contains genes of purine metabolism enzymes, e.g. analogues of hypoxanthine-guanine phosphoribosyl transferase participating in the hypoxanthine reutilization, as well as genes of UA precursor synthesis and XDH transforming xanthine into UA [18]. This bacterium can alter cholesterol absorption in the bowel, decreasing hepatic glycogenesis and enhancing triglyceride synthesis. Collinsella spp. directly correlate with the total cholesterol and low-density lipoprotein levels [19].

Lactobacillus (L.) and Pseudomonas promote UA degradation and excretion in the bowel with SCFA production [9].

L. gasseri PA-3 is a bacterium detected in the yoghurt and other cultured milk products, thus presuming that food habits may affect UA levels [18]. L. gasseri PA-3 may absorb and utilize purines in the bowel, thus decreasing intestinal purine absorption and decreasing serum UA levels [9, 18]. L. brevis DM9218 may efficiently decrease serum UA levels in rats with HU due to the inhibition of xanthine oxidase (XO) activity [9, 20, 21]. L. reuteri TSR332 and L. fermentum TSF331 may control HU via cleaving purines [9].

XDH and XO may be secreted by Escherichia (E.) bacteria in intestinal epithelial cells, accelerate hypoxanthine and xanthine degradation, and transform more purines into UA [9].

The microbial composition also directly affects the cardiovascular system. Some bacteria belonging to Streptococcus and E. coli genera may exhibit proinflammatory effects, producing neurotransmitters in the autonomous nervous system that alter the vascular tone, leading to EH [22], while several L. and Bifidobacterium strains exhibit anti-inflammatory properties and are considered important probiotics [23].

Increased counts of Gram-negative microbes, including Klebsiella, Parabacteroides, Desulfovibrio, Prevotella, correlated with higher BP values. LPS (or endotoxins) form the main component of the outer membrane in Gram-negative bacteria and have proinflammatory properties [14]. Enhanced LPS entering the intestinal

lumen after the cell lysis may promote the production of a large amount of cytokines, enhance the intestinal wall permeability, and cause the low-grade inflammation called "metabolic endotoxemia" [9].

Klebsiella pneumoniae belonging to the Klebsiella genus of the Enterobacteriaceae family, just like other Gram-negative bacteria, may form extracellular vesicles, permeate the intestinal barrier, and migrate to various tissues if the intestinal barrier integrity is impaired due to inflammation, aging, etc. Extracellular vesicles impair the endothelial dysfunction and promote the generation of superoxide anion radicals in endothelial cells, causing endothelial dysfunction [24].

A recent study evaluating the intestinal microbiome alterations in the Chinese population has demonstrated that Desulfovibrio spp. is an obligate anaerobe belonging to sulfate-reducing microbes that breathes anaerobically using sulfate as a final electron acceptor and reducing it to hydrogen sulfide. On the one hand, hydrogen sulfide may become an energy source for mitochondria, while on the other hand it becomes a rather toxic compound in higher concentrations, impairing the intestinal barrier function, elevating the circulating LPS levels, and producing the microbial urease [25, 26].

It has been demonstrated that an atherosclerotic plaque contains a specific microbial medium containing various microbes, e.g. Streptococcus, Pseudomonas, Klebsiella, Veillonella spp., Chlamydia pneumoniae. The comparative intestinal microbiome studies have detected that patients with clinically manifesting atherosclerosis had higher counts of Collinsella spp., Enterobacteriaceae family representatives, Streptococcaceae, along with lower counts of Eubacterium, Roseburia, and Ruminococcaceae producing SCFA compared to healthy persons [14]. Streptococcus may permeate the aortic endothelial cells in humans, stimulating pro-inflammatory cytokines associated with atherosclerosis [19, 27, 28]. Klebsiella and other representatives of the Enterobacteriaceae family are associated with increased tumor necrosis factor α or interleukin-1β levels along with the production of the bacterial metabolite trimethylamine N-oxide (TMAO). In its turn, increased TMAO levels enhance the platelet sensitivity, promoting thrombosis [29].

Veillonella spp. belong to the Bacillota phylum of the Negativicutes class; these affect the formation of atherosclerotic plaques via amino acid fermentation with the production of SCFA [28].

Intestinal Roseburia intestinalis spp., just like Faecalibacterium prausnitzii, are common bacteria producing butyrate due to fiber fermentation.Roseburia intestinalis promotes the metabolic alteration from glycolysis to the use of fatty acids and suppression of systemic inflammation, prevents the formation of atherosclerotic plaques, and slows down atherosclerosis [28, 30].

SCFA effects on CVDs and HU are ambiguous, depending on their type and source. For example, butyrate has cardioprotective properties, while excessive propionate is hazardous in HU. An optimal SCFA balance is important for the body.

Table 1. *The effect of the intestinal microbiota on uric acid levels and cardiovascular risks*

Bacterium	Role in hyperuricemia	Role in cardiovascular diseases
Coprococcus	Butyrate production -> inhibits xanthine dehydrokinase activity -> decreases uric acid levels	Butyrate production -> suppresses low-grade inflammation -> reduces blood pressure
Faecalibacterium prausnitzii	Butyrate production -> inhibits xanthine dehydrokinase activity -> decreases uric acid levels	Decreased synthesis of lipopolysaccharides -> anti-atherosclerotic effect
Collinsella	Produce uric acid, inhibit the degradation of uric acid by other bacteria, and reduce renal and intestinal excretion of uric acid.	Increases triglyceride synthesis, cholesterol and low-density lipoprotein levels
Lactobacillus	Absorbs and utilizes purine in the intestine -> reduces uric acid levels; Inhibits xanthine oxygenase activity	Reduced inflammation -> lower blood pressure
Escherichia	They secrete xanthine dehydrokinase and xanthine oxygenase; they convert purines into uric acid	Neurotransmitter production -> increased blood pressure
Klebsiella	Production of short-chain fatty acids -> breakdown and elimination of uric acid from the body	Impairs endothelial function -> endothelial dysfunction and aging; Found in atherosclerotic plaques; Trimethylamine N-oxide production -> promotes thrombosis
Desulfovibrio	Produces urease	Endotoxin production -> intestinal barrier disruption -> high lipopolysaccharide levels
Veillonella	-	Fermentation of amino acids to form short-chain fatty acids -> formation of atherosclerotic plaques
Roseburia intestinalis	-	Use of fatty acids in metabolism, reduction of systemic inflammation -> prevents the formation of atherosclerotic plaques

Effects of Drug Products on the Microbiome and UA

XO inhibitors are the main pharmacological drugs used in the HU treatment. XO inhibitors decrease UA levels by suppressing the UA synthesis. Allopurinol is a purine XO inhibitor with an active metabolite (oxypurinol) acting as a reversible covalent inhibitor that is excreted with urine. On the contrary, febuxostat is a potent non-purine non-competitive XO inhibitor metabolized in the liver. The recent studies have shown that these drugs not only relieve HU symptoms, but also affect the intestinal microbiome positively. Both drugs could lead to the increased Bifidobacterium counts and decreased pathogenic and/or opportunistic flora counts after decreasing UA levels [9].

SGLT2 inhibitors decrease UA levels due to its enhanced urine excretion and possibly due to the decreased amount of reactive oxygen species that promote UA reabsorption in renal tubules [31].

Alternative Treatment

Thanks to the analyzed mechanisms of microbiome effects on the serum UA levels, the treatment affecting the bacterial count as a specific pathogenetic element is actively searched for (Table 2).

Injecting the Alistipes indistinctus live culture into the body led to the 2.5-fold increase in the UA excretion with feces due to the enhanced production of a hippuric acid metabolite. Hippuric acid may become an alternative treatment of HU and associated metabolic disorders; its biochemical mechanisms are sufficient themselves to restore normal serum urate levels without affecting the renal excretion [11].

Chinese scientists modified the E. coli Nissle 1917 (EcN) probiotic strain for UA cleavage. It demonstrated the ability to cleave UA efficiently both with the oral and intravenous administration. Direct EcN administration into the blood is a new idea for the treatment of metabolic disorders. It has been reported that EcN injections into blood vessels are safe as these do not contain virulence genes and accommodation factors that promote its colonization and survival in the host body [32].

Such microbiome metabolites as polysaccharides beneficially contributed to the UA regulation. During studies, a polysaccharide from Ulva lactuca decreased UA levels, while a polysaccharide from Enteromorpha prolifera significantly decreased serum UA and urea nitrogen levels [9].

Lifestyle modification cannot significantly affect HU, but is a mandatory treatment and metabolic health prerequisite. A Mediterranean diet does not affect the urate level decrease significantly, but is associated with a lower CVD incidence and enhanced life expectancy. With a low-purine diet, serum urate levels decrease approximately by 1 mg/dL. The studies have demonstrated that serum urate levels significantly elevate after the consumption of all alcoholic beverageas, except for wine. Tea and general caffeine consumption were not associated with serum urate levels. An enhanced dairy product consumption was associated with lower serum urate levels [9, 10, 14]. When creating diets for patients with HU, main objective include the limitation of exogenous (food) purines, which somewhat decreased serum UA levels, and the adequate liquid consumption [33].

Sulforaphane, an isothiocyanate obtained from the cabbage family vegetables, has an 80% bioavailability due to its small size and lipophilic origin. In rat experiments it enhanced UA excretion by increasing the renal transporter protein expression and suppressed UA reabsorption decreasing the urate transporter 1 and glucose transporter 9 expression in kidneys. It is also promising that sulforaphane may act as allopurinol, decreasing the XO and adenosine deaminase activity [34].

Table 2. *Comparison of hyperuricemia correction methods*

Method	Mechanism of action	Advantages	Disadvantages
Medicinal products	Direct effect on uric acid metabolism through inhibition of xanthine oxygenase; Increased urinary excretion of uric acid	Fast effect, high efficiency	Side effects
Diet	Reduction of exogenous purines	Security, accessibility, positive impact on other systems	Reduction of uric acid by about 1 mg/dl
Physical exercises	Increased uric acid excretion after exercise	Positive effect on the whole body	During exercise, it temporarily increases uric acid
Fecal microbiota transplantation	Restoring the balance of the microbiota	Long-term effect	Invasiveness, risk of infection, low adherence
Probiotics	Increased excretion of uric acid through the intestine; Breakdown of uric acid	Naturalness, minimum side effects	Survival variability, weak colonization
Postbiotics	Decreased xanthine oxidase activity; decreased uric acid reabsorption, etc.	Stability, dosing, acts immediately	More research is needed

Resveratrol is a flavonoid contained in grapes, wine, and some berries. The mechanism via which resveratrol improves the condition in persons with HU may presume the regulation of the intestinal microbiome composition and function. It is important to note that unlike several animals, humans lack a functional enzyme uricase, i.e. direct uric acid cleavage in the body is impossible. However, the microbiome may affect the intestinal urate excretion, which is one of the methods to decrease UA levels in the body [20].

Physical exercises may lead to the temporary increase in UA levels due to accelerated metabolism, although UA elimination from the serum enhances after training [35].

The effects of probiotics, prebiotics, and fecal microbiome transplant on HU is being currently studied [9].

Probiotics are defined as "viable microbes that are beneficial for the host health when consumed in adequate amounts" [23]. Lactobacillus and Bifidobacterium spp. representatives have been used successfully as probiotics for many years. These bacteria produce lactic acid from carbohydrates, creating an acidic medium that suppresses the growth of several pathogenic bacteria [20].

A single complex large-scale crossover study analyzed the association between the consumption of prebiotics/probiotics and HU in adult US citizens. It has been demonstrated that the consumption of probiotics may decrease serum UA levels. Probiotics upregulate the beneficial flora that has a regulatory role in the metabolism of UA and purines, altering the metabolic balance of amino acids, non-saturated fatty acids, etc., and affects the extrarenal excretion, suppressing the transport of urate transporters in the intestine [2].

Probiotic drugs are considered suitable for modulating the NLRP3 inflammasome signaling pathway to improve HU [9]. Inflammasomes are multimeric protein intracellular platforms that activate in response to infections or tissue injury [36]. HU activates the NLRP3 inflammasome-mediated pyroptosis. Pyroptosis is a form of cellular death characterized by the plasma membrane rupture, cytoplasm swelling, osmotic lysis, DNA cleavage, and a release of a large amount of proinflammatory cytokines [37]. Bifidobacterium spp. may have probiotic effects, suppressing the NLRP3 signaling pathway and NLRP3 mRNA expression. Bifidobacterium spp. are the most important probiotics in the human body, playing a leading role in the prevention of pathogen invasion, mucosal homeostasis, intestinal integrity maintenance, and host immunity regulation [38].

Fecal microbiome transplant (FMT) has recently become a new strategy in HU treatment. FMT presumes transplanting a functional healthy human flora to the patient's gastrointestinal tract in order to form a new intestinal microbiome to treat intestinal and extraintestinal diseases. The mechanism of decreased UA levels in FMT may presume two pathways: accelerated UA decomposition and excretion; effects on UA metabolism with UA transporter regulation in the intestinal epithelium [21].

Treatment Perspectives

The modern medicine is aimed at achieving active longevity of the population. Intestinal microbiome modulation is one of the prospective options to achieve this target, as its composition significantly affects the metabolic health. Thanks to probiotics or other drugs and microbiome effects, it may be possible to decrease the risk of several diseases, decrease polypharmacy, and enhance the treatment efficacy.

A postbiotic (a drug containing non-viable microbes and/or their components that is beneficial for the host health) is one of the promising options. This may be represented by a heterogenous mixture of cellular structures and metabolites, e.g. teichoic acids, exopolysaccharides, peptidoglycans, bacteriocins, etc. [39].

Thus, a G1PB postbiotic was obtained by constant heating of Pediococcus acidilactici GQ01 at 65 °C for 30 minutes. G1PB suppressed the XO activity leading to decreased serum UA, creatinine, and urea nitrogen levels in mice with HU. The drug also regulated the expression of genes and proteins associated with the renal UA reabsorption and excretion [15]. Hippuric acid (see above) is also a postbiotic.

Traditional probiotics demonstrate their potential in decreasing UA levels, although their use is limited due to variable strain survival in the gastrointestinal tract and effects dependent on the colonizing ability [40]. Due to colonization resistance, the majority of probiotics are excreted from the intestine with feces after the oral administration soon after their consumption stops [41]. Postbiotics are a prospective alternative without similar limitations. This can be explained by the larger stability of postbiotics during storage, shipping, consumption, along with a high safety level [42]. Postbiotics may probably form a pathway towards the standardized, safe, and target therapy.

Conclusion

An intestinal microbiome plays a specifically important role in the pathogenesis of HU, which (along with dysbiosis) leads to worse CVD outcomes. Decreased counts of such beneficial bacteria as Coprococcus and Faecalibacterium prausnitzii, as well as the increased counts of pathogenic and/or opportunistic bacteria (e.g., Collinsella, Klebsiella) promote the chronic low-grade inflammation, endothelial dysfunction, and elevated UA levels which worsen cardiometabolic risks.

Prospective correction methods include probiotics modulating purine metabolism and decreasing UA levels; postbiotics that have benefits in stability, efficacy, and suppressed XO activity; FMT restoring the flora balance and thus improving UA excretion; lifestyle modification supplementing the main treatment methods.

Further studies should be aimed at developing innovative personalized therapeutic strategies. The integration of new approaches into clinical practice may promote the improved cardiometabolic health with the decreased polypharmacy rate.

Вклад авторов:

Все авторы внесли существенный вклад в подготовку работы, прочли и одобрили финальную версию статьи перед публикацией

Резник Е.В.: разработка дизайна обзора; написание и редактирование текста рукописи; обзор публикаций по теме статьи; взаимодействие с редакцией в процессе подготовки публикации к печати.

Алиева Л.Х.: обзор публикаций по теме статьи, написание текста рукописи

Фефелова В.А.: обзор публикаций по теме статьи, написание текста рукописи

Кафарская Л.И.: научная консультация, редактирование рукописи

Author Contributions:

All authors made a significant contribution to the preparation of the paper, read, and approved the final version of the article before publication

Reznik E.V.: review design; writing and editing the manuscript; review of publications on the topic of the article; communication with the editors during the publication preparation process.

Alieva L.Kh.: review of publications on the topic of the article, writing the manuscript.

Fefelova V.A.: review of publications on the topic of the article, writing the manuscript.

Kafarskaya L.I.: scientific consultation, editing the manuscript.

Список литературы/ References:

1. Владимиров С.А., Елисеев М.С., Ильиных Е.В., и др., Клинические рекомендации Минздрава России. Подагра, 2018 г. Год обращения 2025г. [Vladimirov S.A., Eliseev M.S., Ilyinykh E.V., Marusenko I.M., Chichasova N.V., Yakupova S.P., Clinical Guidelines of the Russian Ministry of Health. Gout, 2018. Accessed in 2025. (In Russ.)] https://library.mededtech.ru/rest/documents/cr_174/
2. Wang Y, Li S, Li X, et al. (2025) Association between prebiotic, probiotic consumption and hyperuricemia in U.S. adults: a cross-sectional study from NHANES 2011–2018. *Front. Nutr.* 12:1492708. DOI: 10.3389/fnut.2025.1492708
3. Du L, Zong Y, Li H, et al.. Hyperuricemia and its related diseases: mechanisms and advances in therapy. Signal Transduct Target Ther. 2024 Aug 28;9(1):212. PMID: 39191722; PMCID: PMC11350024. DOI: 10.1038/s41392-024-01916-y.
4. Шабалин В.В., Гринштейн Ю.И., Руф Р.Р., и др.. Бессимптомная гиперурикемия: очевидное, спорное, гипотетическое. Профилактическая медицина. 2023;26(7):103-109. [Shabalin VV, Grinstein YuI, Ruf RR, Samsonov NS. Asymptomatic hyperuricemia: obvious, controversial, hypothetical. Russian Journal of Preventive Medicine. 2023;26(7):103-109. (In Russ.)] DOI: 10.17116/profmed202326071103
5. Yanai H, Adachi H, Hakoshima M, et al. Molecular Biological and Clinical Understanding of the Pathophysiology and Treatments of Hyperuricemia and Its Association with Metabolic Syndrome, Cardiovascular Diseases and Chronic Kidney Disease. Int J Mol Sci. 2021 Aug 26;22(17):9221. PMID: 34502127; PMCID: PMC8431537. DOI: 10.3390/ijms22179221.
6. Saito Y, Tanaka A, Node K, et al. Uric acid and cardiovascular disease: A clinical review. J Cardiol. 2021 Jul;78(1):51-57. Epub 2020 Dec 30. PMID: 33388217. DOI: 10.1016/j.jjcc.2020.12.013.
7. Padda J, Khalid K, Padda S, et al. Hyperuricemia and Its Association With Ischemic Stroke. Cureus. 2021 Sep 21;13(9):e18172. PMID: 34703698; PMCID: PMC8530529. DOI: 10.7759/cureus.18172.
8. Xu J, Zhao J, Gu J, et al. Serum uric acid levels as a causal factor in hypertension: Insights from Mendelian randomization analysis. Clin Exp Hypertens. 2025 Dec; 47(1):2496514. Epub 2025 May 5. PMID: 40325623. DOI: 10.1080/10641963.2025.2496514.
9. Wang Z, Li Y, Liao W, et al. (2022) Gut microbiota remodeling: A promising therapeutic strategy to confront hyperuricemia and gout. *Front. Cell. Infect. Microbiol.* 12:935723. DOI: 10.3389/fcimb.2022.935723
10. Danve A, Sehra ST, Neogi T. Role of diet in hyperuricemia and gout. Best Pract Res Clin Rheumatol. 2021 Dec;35(4):101723. Epub 2021 Nov 19. PMID: 34802900; PMCID: PMC8678356. DOI: 10.1016/j.berh.2021.101723.
11. Xu YX, Liu LD, Zhu JY, et al. Alistipes indistinctus-derived hippuric acid promotes intestinal urate excretion to alleviate hyperuricemia. Cell Host Microbe. 2024 Mar 13;32(3):366-381.e9. Epub 2024 Feb 26. PMID: 38412863. DOI: 10.1016/j.chom.2024.02.001.
12. Guo, H., Chen, Y., Dong, W. et al. Fecal *Coprococcus*, hidden behind abdominal symptoms in patients with small intestinal bacterial overgrowth. *J Transl Med* 22, 496 (2024). DOI: 10.1186/s12967-024-05316-2
13. Cheng J and Zhou J (2024) Unraveling the gut health puzzle: exploring the mechanisms of butyrate and the potential of High-Amylose Maize Starch Butyrate (HAMSB) in alleviating colorectal disturbances. *Front. Nutr.* 11:1285169. DOI: 10.3389/fnut.2024.1285169
14. Verhaar BJH, Prodan A, Nieuwdorp M, et al. Gut Microbiota in Hypertension and Atherosclerosis: A Review. Nutrients. 2020 Sep 29;12(10):2982. PMID: 33003455; PMCID: PMC7601560. DOI: 10.3390/nu12102982.
15. Ren L., Wang S., Liu S., et al. Postbiotic Pediococcus acidilactici GQ01, a novel probiotic strain isolated from natural fermented oat juice, attenuates hyperuricemia in mice by modulating uric acid metabolism and gut microbiota. Food. 2024. March 18. 13 (6): 923. PMID: 38540913; PMCID: PMC10969656. DOI: 10.3390/foods13060923.
16. Lopez-Siles M, Duncan SH, Garcia-Gil LJ, et al. Faecalibacterium prausnitzii: from microbiology to diagnostics and prognostics. ISME J. 2017 Apr;11(4):841-852. Epub 2017 Jan 3. PMID: 28045459; PMCID: PMC5364359. DOI: 10.1038/ismej.2016.176.
17. Yang, HT., Jiang, Zh., Yang, Y. et al. Faecalibacterium prausnitzii as a potential Antiatherosclerotic microbe. *Cell Commun Signal* 22, 54 (2024). DOI: 10.1186/s12964-023-01464-y
18. Miyajima Y, Karashima S, Mizoguchi R, et al. Prediction and causal inference of hyperuricemia using gut microbiota. Sci

Rep. 2024 Apr 30;14(1):9901. PMID: 38688923; PMCID: PMC11061287. DOI: 10.1038/s41598-024-60427-6.
19. Choroszy M, Litwinowicz K, Bednarz R, et al. Human Gut Microbiota in Coronary Artery Disease: A Systematic Review and Meta-Analysis. Metabolites. 2022 Nov 23;12(12):1165. PMID: 36557203; PMCID: PMC9788186. DOI: 10.3390/metabo12121165.
20. Zhou Y, Zeng Y, Wang R, et al. Resveratrol Improves Hyperuricemia and Ameliorates Renal Injury by Modulating the Gut Microbiota. Nutrients. 2024 Apr 7;16(7):1086. PMID: 38613119; PMCID: PMC11013445. DOI: 10.3390/nu16071086.
21. Cai JR, Chen XW, He YJ, et al. Washed microbiota transplantation reduces serum uric acid levels in patients with hyperuricaemia. World J Clin Cases. 2022 Apr 16;10(11):3401-3413. PMID: 35611199; PMCID: PMC9048544. DOI: 10.12998/wjcc.v10.i11.3401.
22. Qian B, Zhang K, Li Y, et al.. Update on gut microbiota in cardiovascular diseases. Front Cell Infect Microbiol. 2022 Nov 10;12:1059349. PMID: 36439214; PMCID: PMC9684171. DOI: 10.3389/fcimb.2022.1059349.
23. Zeng L, Deng Y, He Q, et al. (2022) Safety and efficacy of probiotic supplementation in 8 types of inflammatory arthritis: A systematic review and meta-analysis of 34 randomized controlled trials. *Front. Immunol.* 13:961325. DOI: 10.3389/fimmu.2022.961325
24. Li, X., Cui, J., Ding, Z. et al. *Klebsiella pneumoniae*-derived extracellular vesicles impair endothelial function by inhibiting SIRT1. *Cell Commun Signal* 23, 21 (2025). DOI: 10.1186/s12964-024-02002-0
25. Mazidi M, Shekoohi N, Covic A, et al. Adverse Impact of *Desulfovibrio* spp. and Beneficial Role of *Anaerostipes* spp. on Renal Function: Insights from a Mendelian Randomization Analysis. Nutrients. 2020 Jul 25;12(8):2216. PMID: 32722370; PMCID: PMC7468709. DOI: 10.3390/nu12082216.
26. Sun Y., Wu D., Zeng W., et al. (2021) The Role of Arachidonic Acid Metabolism Disorder Caused by Intestinal Dysbiosis in Inflammation in Atherosclerosis. Front. Cell. Infect. Microbiol. 11:618265. DOI: 10.3389/fcimb.2021.618265
27. Sayols-Baixeras S, Dekkers KF, Baldanzi G, et al. *Streptococcus* Species Abundance in the Gut Is Linked to Subclinical Coronary Atherosclerosis in 8973 Participants From the SCAPIS Cohort. Circulation. 2023 Aug 8;148(6):459-472. Epub 2023 Jul 12. PMID: 37435755; PMCID: PMC10399955. DOI: 10.1161/CIRCULATIONAHA.123.063914.
28. Dong Y, Xu R, Chen X, et al. 2023. Characterization of gut microbiota in adults with coronary atherosclerosis. *PeerJ* 11:e15245 DOI: 10.7717/peerj.15245
29. Ortega-Madueño I., Modrego J., Gómez-Gordo R., et al. Relación entre la cuantificación de calcio coronario y la composición de la microbiota intestinal en sujetos sin enfermedad cardiovascular previa: estudio piloto, Clínica e Investigación en Arteriosclerosis, Volume 34, Issue 4, 2022, Pages 205-215, ISSN 0214-9168, DOI: 10.1016/j.arteri.2021.11.008.
30. Wang, Z., Peters, B.A., Bryant, M. et al. Gut microbiota, circulating inflammatory markers and metabolites, and carotid artery atherosclerosis in HIV infection. *Microbiome* 11, 119 (2023). DOI: 10.1186/s40168-023-01566-2
31. You, Y., Zhao, Y., Chen, M. et al. Effects of empagliflozin on serum uric acid level of patients with type 2 diabetes mellitus: a systematic review and meta-analysis. *Diabetol Metab Syndr* 15, 202 (2023). DOI: 10.1186/s13098-023-01182-y
32. Zhao R, Li Z, Sun Y, et al. Engineered *Escherichia coli* Nissle 1917 with urate oxidase and an oxygen-recycling system for hyperuricemia treatment. Gut Microbes. 2022 Jan-Dec;14(1):2070391. PMID: 35491895; PMCID: PMC9067508. DOI: 10.1080/19490976.2022.2070391.
33. Нутрициология и клиническая диетология / под ред. Тутельяна В.А. , Никитюка Д.Б. — Москва : ГЭОТАР-Медиа, 2020. — 656 с. (Серия "Национальные руководства") — ISBN 978-5-9704-5352-0. [Nutrition and Clinical Dietetics / edited by V.A. Tutelyan and D.B. Nikityuk. Moscow: GEOTAR-Media, 2020. — 656 p. (Series "National Guidelines") — ISBN 978-5-9704-5352-0 (In Russ.)]
34. Wang R, Halimulati M, Huang X, et al. Sulforaphane-driven reprogramming of gut microbiome and metabolome ameliorates the progression of hyperuricemia. J Adv Res. 2023 Oct;52:19-28. Epub 2022 Nov 10. PMID: 36371056; PMCID: PMC10555773. DOI: 10.1016/j.jare.2022.11.003.
35. Zhang T, Liu W, Gao S. Exercise and hyperuricemia: an opinion article. Ann Med. 2024 Dec;56(1):2396075. Epub 2024 Aug 26. PMID: 39183708; PMCID: PMC11348809. DOI: 10.1080/07853890.2024.2396075.
36. Лебедев П.А., Волова Л.Т., Осина Н.К., и др. Инфламмасома NLRP3 — новая универсальная мишень терапевтического воздействия у пациентов с бессимптомной гиперурикемией и подагрой. Рациональная Фармакотерапия в Кардиологии. 2024;20(3):331-339. EDN: JQXOBW [Lebedev P.A., Volova L.T., Osina N.K., Paranina E.V. NLRP3 Inflammasome- a new universal target of asymptomatic hyperuricemia and gout management. Rational Pharmacotherapy in Cardiology. 2024;20(3):331-339. EDN JQXOBW (In Russ.)] DOI: 10.20996/1819-6446-2024-3018.
37. Hu Y, Shi Y, Chen H, et al. Blockade of Autophagy Prevents the Progression of Hyperuricemic Nephropathy Through Inhibiting NLRP3 Inflammasome-Mediated Pyroptosis. Front Immunol. 2022 Mar 2;13:858494. PMID: 35309342; PMCID: PMC8924517. DOI: 10.3389/fimmu.2022.858494.
38. Tan, J., Dong, L., Jiang, Z. et al. Probiotics ameliorate IgA nephropathy by improving gut dysbiosis and blunting NLRP3 signaling. *J Transl Med* 20, 382 (2022). DOI: 10.1186/s12967-022-03585-3
39. Ma L, Tu H, Chen T. Postbiotics in Human Health: A Narrative Review. Nutrients. 2023 Jan 6;15(2):291. PMID: 36678162; PMCID: PMC9863882. DOI: 10.3390/nu15020291.
40. Wendel U (2022) Assessing Viability and Stress Tolerance of Probiotics—A Review. *Front. Microbiol.* 12:818468. DOI: 10.3389/fmicb.2021.818468
41. Han S, Lu Y, Xie J, et al. (2021) Probiotic Gastrointestinal Transit and Colonization After Oral Administration: A Long Journey. *Front. Cell. Infect. Microbiol.* 11:609722. DOI: 10.3389/fcimb.2021.609722
42. Корниенко Е.А. Пробиотики, постбиотики и парапробиотики. Экспериментальная и клиническая гастроэнтерология. 2022;205(9): 240-250. PO!: 10.31146/1682-8658-есд-205-9-240-250. DOI: 10.31146/1682-8658-ecg-205-9-240-250

Информация об авторах

Резник Елена Владимировна — д.м.н., доцент, заведующий кафедрой пропедевтики внутренних болезней № 2 Института клинической медицины ФГАОУ ВО РНИМУ имени Н.И. Пирогова, Москва, врач-кардиолог, терапевт, клинический фармаколог, организатор

здравоохранения, врач функциональной и УЗ диагностики ГБУЗ ГКБ № 31 им. Г.М. Савельевой ДЗМ, Москва, elenaresnik@gmail.com, ORCID ID: https://orcid.org/0000-0001-7479-418X

Алиева Луиза Хамидовна — ассистент кафедры пропедевтики внутренних болезней № 2 Института клинической медицины ФГАОУ ВО РНИМУ имени Н.И. Пирогова, Москва, врач-кардиолог отделения реанимации и интенсивной терапии № 3 ГБУЗ «ГКБ № 67 им. Л.А. Ворохобова ДЗМ», Москва, luizaalieva94@mail.ru, ORCID ID: https://orcid.org/0009-0007-0647-2761

Фефелова Валерия Александровна — врач ординатор терапевт кафедры пропедевтики внутренних болезней № 2 Института клинической медицины ФГАОУ ВО РНИМУ имени Н.И. Пирогова, Москва, fefeloval98@gmail.com ORCID ID: https://orcid.org/0009-0008-5335-8803

Кафарская Людмила Ивановна — д.м.н., профессор, заведующий кафедрой микробиологии и вирусологии ИПМ, ведущий научный сотрудник НИЛ микробиологии и биологической безопасности ИПМ.

Author information

Elena V. Reznik — MD, assistant professor, Head of the Department of Propedeutics of Internal Diseases of the medical faculty of the Russian national research medical University named after N.I. Pirogov of the Ministry of healthcare of the Russian Federation, Moscow; Cardiologist of the City Clinical Hospital N31 of Healthcare Department of Moscow, elenaresnik@gmail.com, ORCID ID: https://orcid.org/0000-0001-7479-418X

Luiza H. Alieva — assistant of the Department of Propedeutics of Internal Diseases of the medical faculty of the Russian national research medical University named after N.I. Pirogov of the Ministry of healthcare of the Russian Federation, Moscow; Cardiologist of the Moscow Department of Health L.A. Vorokhobov City Clinical Hospital No. 67, Moscow, luizaalieva94@mail.ru, ORCID ID: https://orcid.org/0009-0007-0647-2761

Valeria A. Fefelova — is a resident physician and internist at the Department of Propaedeutics of Internal Diseases of the medical faculty of the Russian national research medical University named after N.I. Pirogov of the Ministry of healthcare of the Russian Federation, Moscow. fefeloval98@gmail.com ORCID ID: https://orcid.org/0009-0008-5335-8803

Lyudmila I. Kafarskaya — Doctor of Medical Sciences, Professor, Head of the Department of Microbiology and Virology at the Institute of Microbiology, Leading Researcher at the Research Laboratory of Microbiology and Biological Safety at the Institute of Microbiology

Автор, ответственный за переписку / Corresponding author