Metabolic mechanism of dietary factors and effect of dietary types associated with hyperuricemia: A review

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ABSTRACT: Globally, hyperuricemia is a growing health, social, and economic problem which could cause gout, chronic kidney diseases and other diseases. There are increasing evidences that a sensible diet makes sense to reduce the risk of hyperuricemia. This review aims to explore the metabolic mechanism of dietary factors and effects of dietary types associated with hyperuricemia. Recommendations for dietary modification to prevent hyperuricemia are as following: decreasing intake of animal organs, seafood, sugar-sweetened, and alcohol beverages is essential; choosing water or unsweetened tea and coffee instead of sweetened beverages is beneficial; and increasing intake of vegetables, reduced-fat dairy products, foods containing fiber, micronutrients and unsaturated fatty acids is helpful. In addition, consumption of fruits and legumes in moderation is advantageous, and low-fructose of fruits and low-purine of non-soy beans are recommended. Moreover, personalized diet needs to be emphasized for hyperuricemic patients accompanied with diverse metabolic diseases.

Keywords: Purine; Metabolic mechanism; Dietary types; Hyperuricemia; Personalized diet

1. Introduction

Hyperuricemia is a chronic metabolic disease due to the disorders of purine metabolism and decreased urate excretion or urate overproduction, and is closely associated with gout. The clinical features of hyperuricemia are that excessive uric acid generated by human body is deposited in the joints and peripheral tissues, resulting in crystallization [1]. At present, in addition to hypertension, hyperlipidemia, and hyperglycemia, hyperuricemia has become the "fourth highest" disease. Moreover, hyperuricemia is an independent risk factor for obesity, dyslipidemia, non-alcoholic fatty liver disease, diabetes, metabolic syndrome, heart failure, chronic kidney diseases, cardiovascular diseases and stroke [2,3]. Meanwhile, these diseases are also complications of hyperuricemia (Fig.1). The diagnostic criteria for hyperuricemia are as

follows: serum urate is higher or equal to 360 μmol/L in females and 420 μmol/L in males [4]. It has been most commonly found that long-term hyperuricemia can lead to uric acid crystals deposited in joints and other parts of the body, and thus can cause gout if it is not well controlled. The occurrence of hyperuricemia in Chinese adults was 11.1% in 2015-2016 while it was increased to 14.0% in 2018-2019 [5]. According to data from the White Paper on Trends of hyperuricemia and gout in China in 2021-2022, the overall prevalence of hyperuricemia in China is 13.3%.
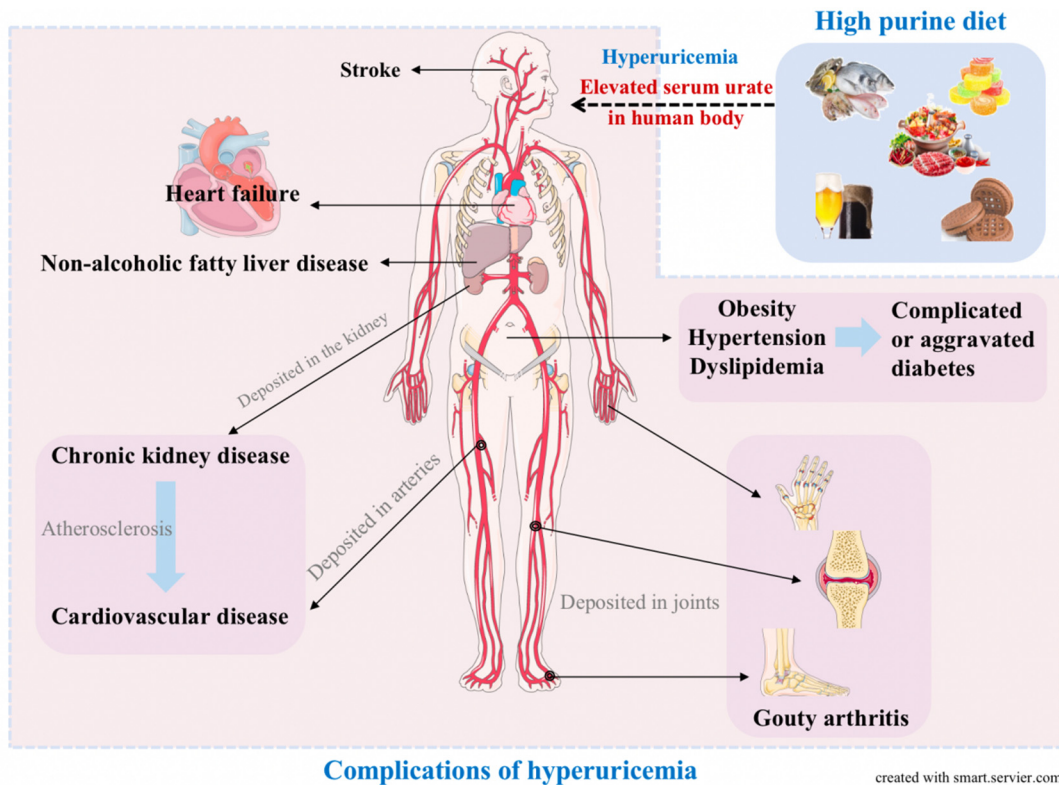

Fig. 1. Hyperuricemia and its complications.

Currently, the treatment of hyperuricemia primarily includes two aspects: one is to treat hyperuricemia flares and quickly relieve the related symptoms, and another is that long term uric acid reducing therapy should be performed to restrain the occurrence of gout flares or other complications [6,7]. Although there are already some drugs used for the therapy of hyperuricemia and gout like allopurinol, benzbromarone, glucocorticoids, colchicine, febuxostat, interleukin-1 inhibitors and polyethylene glycol uricase (PEG uricase) [1,7]. However, some drugs have side effects, for example, patients with hyperuricemia may cause skin allergies when treated with allopurinol [8], and benzbromarone has been banned in the European market as it could cause damage to the liver after it is metabolized [9]. Thus, it is essential to prevent the occurrence of hyperuricemia from dietary intervention. A reasonably and selective diet makes sense to lessen the risk of developing hyperuricemia [10]. Besides, personalized diet for hyperuricemia patients accompanied with diabetes, chronic kidney diseases, non-alcoholic fatty liver disease, cardiovascular disease and other different metabolic diseases should be taken seriously. According to the guideline of 2020 American College of Rheumatology and British Society of Rheumatology for gout management, the high consumption of red meats, organ meats, seafood, alcoholic beverages and sugar-sweetened drinks are a vital risk factor for the

increased SUA levels and could increase the risk of hyperuricemia. However, vitamin C, dairy products, vegetables, dietary fiber and micronutrient-rich foods could lower the risk of hyperuricemia [11,12]. In addition, patients are also encouraged to drink adequate water, including tea and coffee, to at least 2,000 mL per day [4]. Therefore, a reasonable diet is essential to prevent the formation of hyperuricemia.

The research trends and topics of diet on hyperuricemia in selected 800 references which searched in Web of Science during last three decades (1990–2022) were summarized via VOSviewer software (version 1.6.18, Leiden University, Leiden, The Netherlands). The minimum frequency of keywords occurrence was set as 20, and the clustering co-occurrence map was drawn. The results of bibliometrics and visualization analysis could objectively list the current research status, hotspots, development background and expected research topics in this direction. Each circular node represents a keyword, the line represents the co-occurrence relationship between the two keywords, and the color of the node represents different clusters. The results of network visualization are presented in Fig. 2. The research surrounding diet on hyperuricemia includes these aspects: the different study populations (male and female, different countries), themes around foods include meat, vegetables, fruits, sugar, alcohol, milk, coffee and so on. In addition, these researches also addressed the complications of hyperuricemia.

Fig. 2. Network visualization of the titles and abstracts in selected 800 references related to the topics of diet on hyperuricemia from 1990–2022.

Given the increasing incidence of hyperuricemia worldwide, the potential side effects of drug therapy and the current research progresses, this comprehensive review aims to discuss the metabolic mechanism of dietary factors associated with hyperuricemia in terms of dietary types, thereby providing a meaningful dietary guideline to decrease the risk of hyperuricemia, reducing exogenous purine intake and blood uric acid load, delaying the development of hyperuricemia related complications. We emphasize prevention before hyperuricemia disease occurs, and also suggest the differences in personalized diet and precise dietary options for hyperuricemia patients accompanied with different metabolic diseases, thus promoting the appropriate nutritional status of human body.

2. The occurrence mechanism of hyperuricemia

Under normal physiological conditions, purine production and catabolism are in a relatively stable equilibrium of 300 to 400 mg per day [13]. When this balance is broken, serum urate levels significantly increase, resulting in the occurrence of hyperuricemia. Almost all uric acids are filtrated through the glomerulus, and then renal tubules regulate uric acid excretion through reabsorption and secretion. Reabsorption and secretion of approximately 90% of uric acid occurs in proximal renal tubule, and this process regulates uric acid levels by exchanging intracellular anions for uric acid transporters. Approximately 10% of uric acid is percolated out of body as urine at the distal end of proximal renal tubule. A small amount of the remaining uric acid is filtered out through gut. The details about this process are summarized in Fig. 3 [13,14]. The absorption and transport of SUA is adjusted through uric acid transporters which exist in the kidneys and intestinal tract, including urate transporter 1 (URAT1), organic anion transporters (OATs), sodium-dependent phosphate transporter 1 (NPT1), glucose transporter 9 (GLUT9), glucose transporter 12 (GLUT12) and ATP-binding cassette subfamily G member 2 (ABCG2) [10,15]. URAT1 is a membrane protein in the OATs family located on proximal renal tubular epithelial cells [16]. As a key channel for regulating blood uric acid level, URAT1 can specifically bind to urate, and hyperuricemia is manifested by the upregulation of URAT1. NPT1 is also one urate transporter in the kidney [15]. Besides, GLUT9 participates in uric acid reabsorption across renal tubular epithelial cells. It is not only involved in glucose transport, but also a urate transporter, which plays a vital role in uric acid production and excretion. Other study has shown that GLUT12 was also involved in the process of uric acid reabsorption [17]. ABCG2 is present in the apical membrane of kidney and intestinal epithelial tissue as a multi-specific transporter with high volume transportation activities, and plays an important physiological character in uric acid secretion in kidney and gut [18]. In conclusion, as a basic target for hyperuricemia therapy, uric acid transporters make sense in the process of uric acid metabolism. By upregulating the expression of uric acid secretory proteins and downregulating the expression of reabsorption proteins, the body accelerates uric acid excretion.
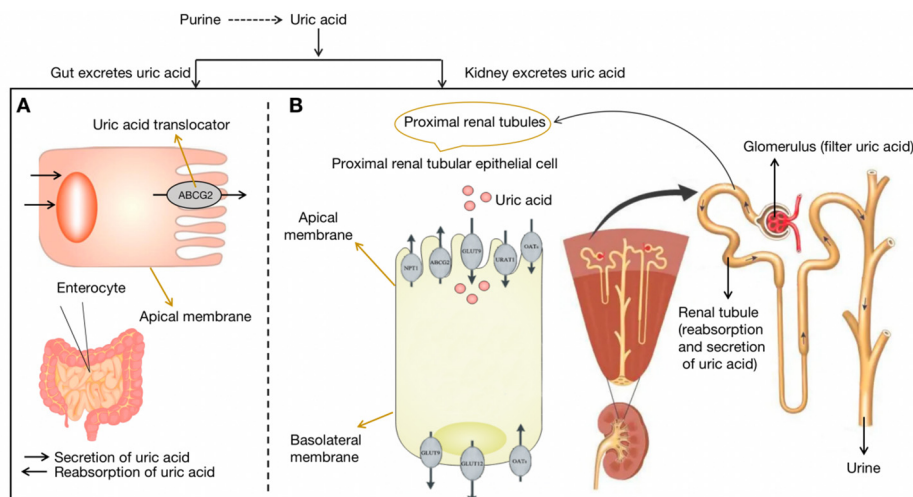

Fig. 3. Excretion of SUA in human body (A: gut excretes uric acid; B: kidney excretes uric acid; ABCG2: ATP-binding cassette subfamily G member 2; URAT1: urate transporter 1; OATs: organic anion transporters; GLUT9: glucose transporter 9; GLUT12: glucose transporter 12; NPT1: sodium-dependent phosphate transporter 1).

3. Metabolic mechanism of dietary factors associated with hyperuricemia

3.1. Metabolic mechanism of dietary factors increasing the risk of hyperuricemia

3.1.1. Purine

Purines are mainly nucleotides found in food, mainly in the form of purine nucleotide, which can be divided into hypoxanthine, adenine, xanthine and guanine. Purines are important components of nucleic acids, coenzymes and other biological molecules and have been shown to be involved in nerve transmission, which are widely involved in various life activities of the human body [19]. Sources of purines in the human body include endogenous and exogenous purines, during the process of purine metabolism in human body, senescent cells are continuously removed, and in the process of apoptosis, nucleic acids are oxidized and degraded to produce large amounts of purines (endogenous purines). Those ingested through foods are called exogenous purines. The details of purine metabolism are shown in Fig. 4. The final product of endogenous and exogenous purine metabolism is uric acid. The 80% of uric acid generates from endogenous purine metabolism and 20% comes from exogenous purine metabolism in the body [20]. Under the action of xanthine oxidoreductase (XOR), hypoxanthine is oxidized to xanthine, and then xanthine is eventually oxidized to uric acid [19]. Two thirds of uric acid from purine metabolism is egested through the kidneys, and one third from the intestinal excretion [21]. Serum uric acid (SUA) overproduction or inadequate excretion could lead to the formation of sodium urate crystals which are deposited in the kidneys, joints, and other tissues, with the potential to further develop into gout. Although exogenous purine intake accounts for a small proportion, as a factor that individuals can control and regulate initiatively, more and more studies have concerned the effect of diet on hyperuricemia. Diet occupies an integral role in the generation or suppression of hyperuricemia, leading to an increased production of urate through the contribution of purines in the diet. There have been many studies demonstrating that food intakes with high purine contents are concerned with a higher risk of hyperuricemia [22,23].
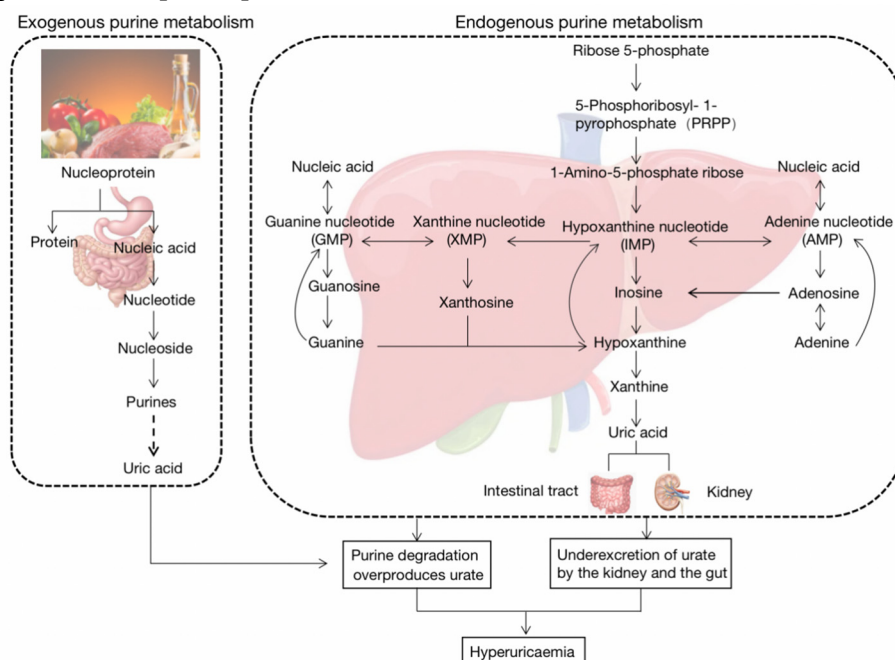

Fig. 4. Purine metabolism in human body.

3.1.2. Fructose

Fructose is an energy source that includes both natural fructose existing in foods combined with fiber, vitamins and minerals, and synthetic fructose (such as high fructose corn syrup) is added independently in processed foods [24]. Fructose could cause oxidative stress in mitochondria and restrain the activity of adenosine monophosphate activated protein kinase (AMPK), with the depletion of adenosine triphosphate (ATP) and nucleotides in cells, leading to an increase in SUA and an increased risk of hyperuricemia and gout [25]. Jang et al. studied the metabolic path of fructose in human body by using isotope tracer method and mass spectrometry, and found that a low-dose fructose (<0.5 g/kg) could be eliminated by 90% of the intestinal tract, while a high-dose fructose (>1 g/kg) could block the absorption and clearance of fructose by the gut, leading the fructose to arrive at the intestine and liver [26]. The glucose transporter type (GLUT) family makes up of 14 members, seven of which are capable of transporting fructose (GLUT2, GLUT5, GLUT7, GLUT8, GLUT9, GLUT11 and GLUT12) simultaneously, while GLUT5 is the only transporter specific to fructose [24]. The detailed process of fructose metabolism in the human body is shown in Fig. 5. GLUT5 transports dietary fructose to the small intestine, and fructose metabolism begins in the small intestine epithelium, and then is metabolized in the liver. Fructokinase converts fructose to fructose-1-phosphate, then decomposes with fructokinase into glyceraldehyde and dihydroxyacetone phosphate, and eventually produce CO_2 and fatty acid [27,28]. This process is also accompanied by the energy release, and adenosine diphosphate (ADP) is broken down by nucleoside monophosphate kinase into adenosine monophosphate (AMP), which is then processed under many kinds of enzymes to generate uric acid, and hyperuricemia occurs when uric acid in the blood reaches a certain level.
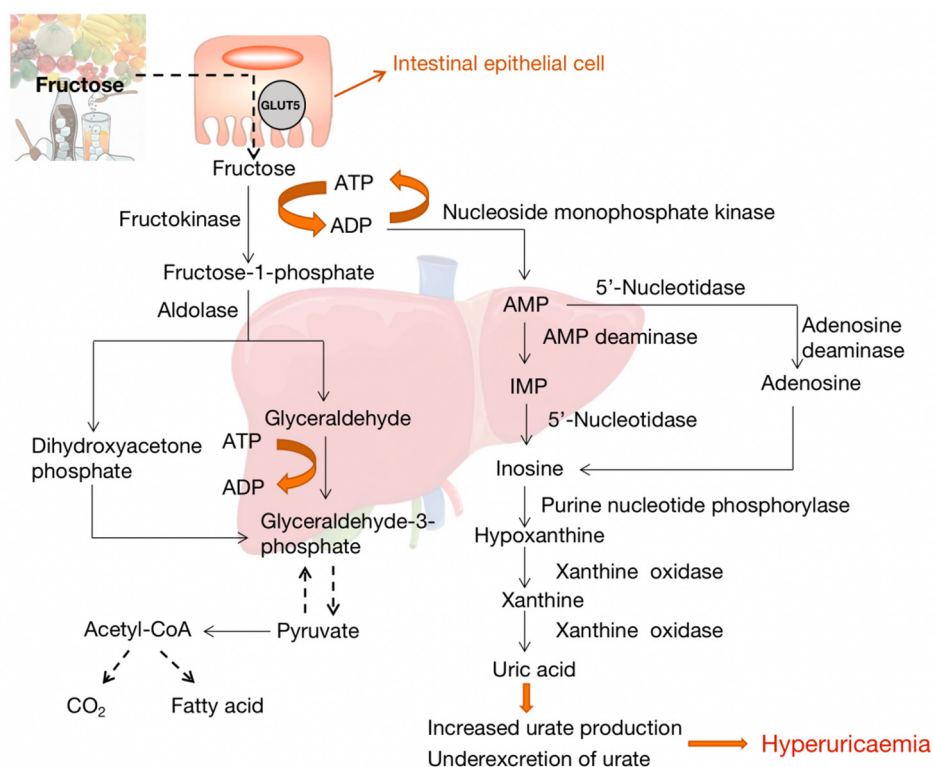

Fig. 5. Fructose metabolism in human body (GLUT5: glucose transporter type 5; ATP: adenosine triphosphate; ADP: adenosine diphosphate; AMP: adenosine monophosphate; IMP: inosine monophosphate).

3.1.3. Alcohol

Liver is the main organ for alcohol metabolism in human body. The metabolites produced during alcohol metabolism could lead to liver damage and cause alcoholic liver disease through various mechanisms like disrupting lipid metabolism, increasing inflammatory response and causing fibrosis [29]. The detailed process of alcohol metabolism in human body is shown in Fig. 6. Heavy alcohol consumption increases SUA levels and produces excessive uric acid through adenine nucleotide degradation, and increased lactate inhibits uric acid excretion in the kidneys, thus increasing the risk of hyperuricemia. On the one hand, alcohol enters the body by absorption, which oxidizes ethanol to acetaldehyde in the liver and promotes the production of nicotinamide adenine dinucleotide (NADH). At the same time, this process also facilitates the conversion of pyruvate to lactate, and lactate can inhibit uric acid excretion in the kidney. Besides, URAT1 can reabsorb uric acid and secrete lactic acid, which reduces the rate of uric acid excretion in the body, resulting in hyperuricemia [30]. Alcohol consumption inhibits renal uric acid excretion by increasing serum lactate concentration. Specifically, serum lactate is exchanged with urate through sodium-dependent monocarboxylic acid transporters (SLC5A9 and SLC5A12), which inhibits renal tubule excretion via activating the exchange function of URAT1 [31]. On the other hand, during the alcohol metabolism, alcohol is dissolved into acetaldehyde after it is absorbed in the stomach and reaches the liver. Acetaldehyde is broken down into acetic acid by aldehyde dehydrogenase and later into acetyl AMP, and finally, acetyl AMP generates acetyl CoA under the action of coenzyme A, along with the release of energy (ATP is dephosphorylated to AMP). As a result, the concentration of purines (e.g., hypoxanthine, xanthine) in the serum increases, and subsequently uric acid concentration also increases, ultimately resulting in hyperuricemia.
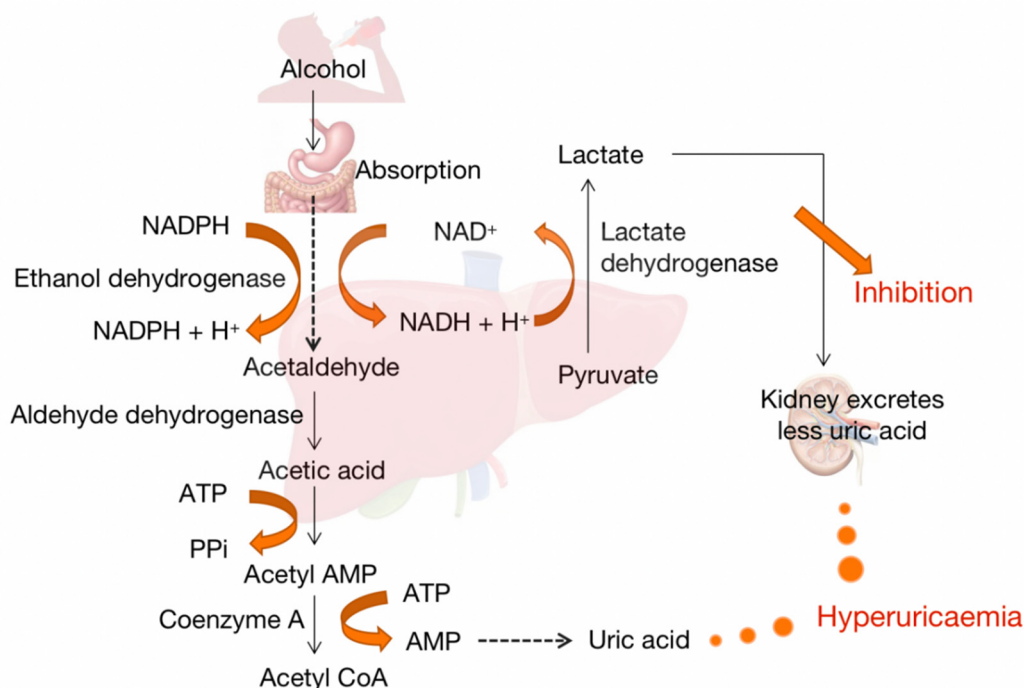

Fig. 6. Alcohol metabolism in human body (NADPH: nicotinamide-adenine dinucleotide phosphate; NADH: nicotinamide-adenine dinucleotide; PPi: inorganic pyrophosphate; ATP: adenosine triphosphate; AMP: adenosine monophosphate).

3.2. Metabolic mechanism of dietary factors decreasing the risk of hyperuricemia

3.2.1. Water

Water is essential for body metabolism. Impaired renal function affects uric acid excretion and is a factor causing hyperuricemia. The metabolic mechanism of water in human body may be as follows: drinking plenty of water helps with uric acid excretion, especially for people with renal dysfunction, and increased urine volume can reduce the concentration of uric acid in the urine, preventing excessive uric acid from causing urinary stones. Based on the dietary guideline for patients suffered from hyperuricemia and gout made by China Health Industry Standard, it is recommended to drink 2,000 mL water (including tea and coffee) each day for people with hyperuricemia and gout symptoms [4]. In addition, according to the British Society of Rheumatology guidelines of the treatment for patients with gout, patients are suggested to drink 2 L of water daily [12]. Expect regular drinking water, other types of water have also been reported to lower SUA levels, such as alkaline drinking water, oxygenated water and electrolytic drinking water. Yu et al. reported that drinking alkaline drinking water (pH = 9.0) could reduce the risk of hyperuricemia and acute kidney injury for mice, as this water can act on urate anion transporter URAT1 which is located in the proximal renal tubules of mice, inhibit the expression of URAT1 mRNA, thereby decreasing the renal reabsorption of urate, and ultimately lowering the SUA level [32]. Hyperuricemic rats treated with oxygenated water had a marked improvement in the production of uric acid, and could decrease SUA level and a slow increase rate of SUA, which was due to that the high oxygen concentration enhanced the rate of oxygen uptake, promoted the glycolytic process, increased mitochondrial protein synthesis [33]. Shi et al. (2020) studied that rats with hyperuricemia were given electrolytic drinking water and showed that uric acid excretion significantly increased with the intake of electrolytic drinking water [34]. Therefore, adequate drinking water (about 2,000 mL per day) can lower SUA levels and reduce the risk of hyperuricemia, which is also be beneficial for patients suffered from hyperuricemia.

3.2.2. Vitamin C

Vitamin C is necessary for the prevention of scurvy in humans and has been relevant to the prevention of many common diseases, such as coronary heart disease, myocarditis, stroke, atherosclerosis and cancer, as well as enhancing the antioxidation and strengthening the immune system [35]. Previous researches have shown a vital negative relation between vitamin C intake and SUA levels. The inferred metabolic mechanism is as follows: vitamin C promotes uric acid secretion via suppressing the reabsorption function of uric acid transporters URAT1, SLC5A9 and SLC5A12 in the proximal tubule, and these transporters increase the renal clearance of uric acid. At the same time, vitamin C reduces the damage of free radicals to the cells of the body, thereby reducing SUA levels [31]. Moreover, vitamin C has been reported to play a vital role in reducing urate-induced inflammation by inhibiting the activation of the nod-like receptor protein 3 (NLRP3) inflammasome which is responsible for the treatment of urate-induced inflammation [36]. A daily of 500 mg vitamin C supplements for two months could dramatically reduce SUA levels among patients with hyperuricemia [37]. Furthermore, vitamin C supplements with 500-1,500 mg each day have

also been reported to reduce SUA concentration [11]. A meta-analysis from one published randomized controlled trial reported that supplementation of vitamin C reduced SUA levels for patients with asymptomatic hyperuricemia who did not progressed to gout, and the SUA reduction was greater in trials where vitamin C was given 500 mg/day [38]. Vitamin C intake has an active impact on purine metabolism, helping reduce uric acid levels and thereby decreasing the risk of sodium urate crystals deposition in joints and soft tissues to develop gout.

3.2.3. Other dietary micronutrients

Micronutrients are important components of diet, and play a vital role in body metabolism and maintenance of body tissue function. In the human metabolic pathway, if there is a lack of one key micronutrient, the complex chemical reactions in body may not be able to proceed smoothly and the normal metabolism will be disrupted, thus affecting the health of the human body and causing illness [39]. There have been some studies linking dietary micronutrient intake to hyperuricemia, and the metabolic mechanism of different kinds of micronutrients on hyperuricemia are diverse. For example, vitamin D deficiency can activate human parathyroid glands and stimulate the release of parathyroid hormones, while SUA levels rise with elevated serum parathyroid hormone concentrations. Thus the supplementation vitamin D can reduce the concentration of SUA [40], this result was also demonstrated by Zhang et al., which reported that dietary vitamin D, vitamin D supplements and total vitamin D intake were significantly correlated with hyperuricemia among American adult males who evaluated from the Survey of National Health and Nutrition Examination ranged from 2007 to 2014 [41]. Dietary magnesium consumption was negatively correlated with serum C-reactive protein level, whereas hyperuricemia is positively associated with serum C-reactive protein and considered as a known inflammation biomarker, so a lack of dietary magnesium consumption could increase the risk of hyperuricemia [42]. Also, previous study has shown that dietary iron intake higher than 11 g/d was correlated significantly with reduced uric acid levels of 10-30 μmol/L [43], while intake of dietary zinc was highly associated with hyperuricemia which might be attributed to the antioxidant properties of zinc [44]. Folic acid supplementation also helped to reduce SUA concentration by decreasing the activity of xanthine oxidoreductase which is the crucial enzyme responsible for the oxidation of hypoxanthine to xanthine [45]. According to the present researches, encouraging dietary intake of some micronutrient-rich foods (such as vegetables, fruits, grains, nuts, spices and coffee) can be beneficial to lower the SUA concentration and decrease the risk of hyperuricemia.

3.2.4. Unsaturated fatty acids

Unsaturated fatty acids (UFAs) can maintain the normal physiological function of cells, control lipid levels, and reduce cholesterol and triglycerides in the blood and protect blood vessels. In addition, UFAs also show a better uric-acid lowering effect, especially the long chain UFAs has a greater inhibitory impact on uric acid transporter URAT1 than saturated fatty acids (SFAs). Among UFAs, omega-3 fatty acids are more suitable for preventing hyperuricemia and could be used as more effective URAT1 inhibitors compared with omega-6 fatty acids. α-Linolenic, docosahexaenoic acid (DHA) and eicosapentaenoic acid

(EPA) showed the stronger URAT1 inhibitory activities among omega-3 fatty acids [46]. Moreover, study has shown that UFAs can reduce uric acid and protect against kidney injury, and its mechanism is mainly manifested by suppressing the xanthine oxidase activity in purine metabolism, and down-adjusting the presentation and excretion of proinflammatory factors (IL-1β, IL-6, IL-18, MCP-1 and TNF-α) induced by hyperuricemia. On the other hand, UFAs regulate protein expression associated with uric acid transporter, such as GLUT9, URAT1 and OAT1, and may relieve renal injury caused by hyperuricemia through recovering the Keap1-Nrf2 pathway and preventing the activation of thioredoxin-interacting protein/nod-like receptor protein (TXNIP/NLRP3) inflammasome [47]. Therefore, dietary intake of foods rich in UFAs is recommended to reduce the level of SUA, so as to prevent the occurrence of hyperuricemia.

3.2.5. Other dietary factors

In addition to vitamin C, micronutrients, and unsaturated fatty acids, other dietary factors may also reduce the risk of hyperuricemia, such as (1) bioactive compounds derived from natural foods including polyphenols and saponins, can significantly inhibit the activities of key enzymes in uric acid synthesis, thus achieving the effect of lowering uric acid [48-51]. (2) peptides from food sources can lower uric acid by inhibiting the activity of xanthine oxidase [52]. The flavonoids extracted from corn silk reduced the SUA level of oxonate potassium induced hyperuricemia mice by inhibiting xanthine oxidase activity and promoting SUA excretion [50]. Ferulic acid can be used as a dietary agent for the treatment of metabolic syndrome-associated hyperuricemia due to its blocking effects of elevated uric acid synthetase activity and mRNA expression induced by high fructose and high fat diets [53]. The anti-hyperuricemia mechanism of saponins is mainly through the down-regulation of URAT1 and GLUT9 transporters, and the up-regulation of OAT1 and OAT3 transporters [54]. Moreover, WPPKN (640.8 Da) and ADIYTE (710.7 Da), two anti-hyperuricemia peptides obtained by separation, purification and identification of walnut meal hydrolysate, were proved to have a high xanthine oxidase inhibitory activity *in vitro*. WPPKN entered into the hydrophobic channel and blocked the interaction between xanthine and xanthine oxidase, however, ADIYTE sited on the B-chain surface which blocked the substrate's entry into the hydrophobic channel according to molecular docking thus exerting anti-high uric acid properties [55].

4. Effect of dietary types associated with hyperuricemia

4.1. Some foods intake increases the risk of hyperuricemia

4.1.1. Meats

The meats mentioned in this review refers to livestock and poultry meats (red meats, white meats and organ meats). Red meats, including beef, pork and lamb, are long entrenched as a crucial source of dietary protein, fatty acid and some important micronutrients such as vitamin, iron and zinc, but researches have also shown that its overconsumption can increase the risk of cardiovascular disease, NAFLD, colon cancer, and hyperuricemia [56]. Organ meat mainly includes animal offal, such as the liver, kidney, heart and sweetbread. Besides, compared with plant-derived proteins, animal-derived proteins are definitely related

with the prevalence of hyperuricemia, especially for red meats and organ meats [23]. The content of protein in meat is high which also contains lots of purines. Excessive intake of dietary purine greatly increases the risk of hyperuricemia in human body as the dysfunction of purine metabolism (see Fig.4) is the main cause of hyperuricemia. Besides, increased SUA levels from red meat intake are associated with high levels of saturated fatty acids which are positively associated with insulin resistance, and insulin resistance reduces uric acid excretion by the kidneys, thus leading to the occurrence of hyperuricemia [57]. Higher levels of meat consumption were associated with higher SUA levels because of the higher purine contents, but total dietary protein intake was not [58]. The purine contents in different meat are shown in Fig.7. According to the results of Pan and Kaneko's determination of purine contents in different foods, food with purine content less than 50 mg/1kg is defined as the low purine food, purine content ranging from 1,000 to 2,000 mg/kg is defined as the medium purine food, and food with purine content more than 2,000 mg/kg is defined as the high purine food [59-61]. Animal organs contain more purines than red meat and white meat among all kinds of meats, and liver has the highest purine content, followed by kidney and heart. Among chicken, breast meat has the highest purine content at 2,079.7 mg/kg, followed by chicken gizzard (1,429.0 mg/kg) and chicken wing (1,375.0 mg/kg). Among pork, pork rump has the highest purine content at 1,507.3 mg/kg, followed by pork tenderloin (1,447.5 mg/kg) and pork fore hock (1,293.7 mg/kg). The purine contents of mutton and duck are 1,090.9 mg/kg and 962.2 mg/kg, respectively. The animal sourced food intake is positively linked with the risk of hyperuricemia, and limiting the intake of animal food is more beneficial to the hyperuricemic patients. Thus, individuals accompany with high SUA levels need to avoid large amounts of meat intake in their daily diet, especially organ meats and red meats.
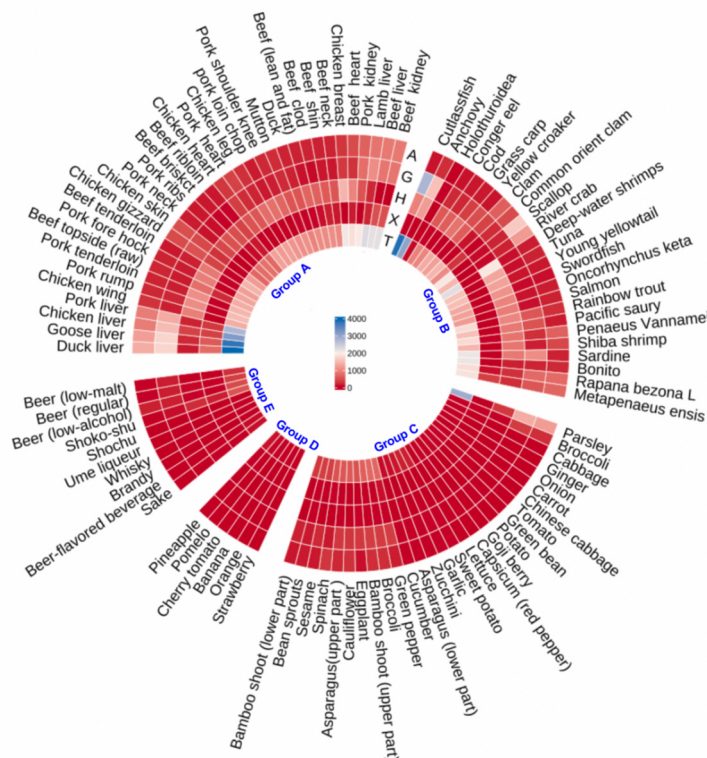

Fig. 7. Purine contents in different foods items (purine contents (mg/kg, μmol/L for alcoholic beverages) verified from the references [59-64], all the data are shown in Table S1. A: Adenine; G: Guanine; H: Hypoxanthine; X: Xanthine; T: Total purine; Group A: meats; Group B: aquatic products; Group C: vegetables; Group D: fruits; Group E: alcoholic beverages).

4.1.2. Seafood

Seafood (fish and shellfish harvested from marine and freshwater environments or aquaculture production), with low fat, rich in protein and vitamins, and delicious taste, is an important part of a reasonable diet [65]. However, the intake of seafood has been well known to increase the risk of hyperuricemia as seafood contains the higher purines [22,23]. The purine contents in different seafood are shown in Fig. 7. According to Pan and Kaneko's measurement [59-61], the purine content of cutlassfish was the highest with 3,854 mg/kg, followed by anchovy at 3,039 mg/kg and deep-water shrimps at 2,216 mg/kg. The purine content of scallop and metapenaeus ensis was 1,934.4 mg/kg and 1,875 mg/kg, respectively. Cod had the least purine content with 980 mg/kg. According to the determination of purine contents in seafood by Qu et al. [64], the total contents of purine in shrimp was the highest, followed by fish and bivalves. Villegas et al. [23] claimed the connection between the prevalence of hyperuricemia and high purine food intake among 3,978 males aged 40-74 years, revealing an intensely positive association between seafood intake and hyperuricemia. In addition, an extra serving of seafood per week added the risk of gout by 7% [31]. Higher seafood intake leads to more severe clinical outcomes in patients who already have gout, as in most gout patients, renal uric acid clearance is relatively impaired and the absorption of purines in the diet generates a dramatic increase in SUA levels. Considering the high purine contents of seafood, as well as the clinical dietary guidance for patients suffered from hyperuricemia and gout, it would be better for patients to avoid excessive fish and shrimp consumption, such as cutlassfish, bonito, anchovy, sardine, deep-water shrimp, metapenaeus ensis and scallop.

4.1.3. Sugar-sweetened foods

Sugar-sweetened foods (SSFs) include sugar-sweetened beverages (carbonated or noncarbonated beverages, fruit drinks, sport drinks, sodas, soft drinks and sweetened coffee or tea, energy and vitamin drinks) and sugar-sweetened processed foods (succade, preserved fruit, candy, chocolate, cake, biscuits and pastries), which have become the main dietary source of added sugars around the world. In daily life, most of the increased fructose intake comes mainly from processed sugary foods. The harmful impacts of a high fructose intake on human health have long been a concern for consumers and the scientists including a high risk of obesity, hypertension, diabetes and cardiovascular disease. A high fructose intake could lead to insulin resistance, increase the levels of blood glucose after meals and improve the concentration of triglycerides in blood, as well as SUA concentrations [27]. Moreover, a high fructose intake is associated with increased levels of SUA [25,66,67]. Sugar-sweetened beverages (SSBs), soft drinks and excessive dietary fructose consumption were related with increased risk of hyperuricemia among adults and adolescents [68,69]. Studies have demonstrated that High intake of sugar-sweetened soft beverages with a 30% in man (40% in woman) added risk of hyperuricemia, however, unsweetened juice intake was not related with either a relatively higher risk of hyperuricemia and SUA levels because it contained more plant bioactive compounds like dietary polyphenols, vitamin C, flavonoids and so on [69]. This also proved that fructose from food sources has a lower burden on uric acid metabolism than pure fructose [70]. Therefore, it

is recommended to consume restricted sugar-sweetened foods, reduce the intake of sugar-sweetened processed foods, and increase the intake of fructose from natural dietary sources, which would be useful to decrease the risk of hyperuricemia.

4.1.4. Alcoholic beverages

Alcoholic beverages are those with an alcohol content of 0.5% vol or more, including fermented and distilled alcoholic beverages, integrated alcoholic beverage, as well as non-alcohol beer and non-alcohol wine [71]. Compared to meat and aquatic products, alcoholic beverages contain less purine, but alcohol consumption produces excessive uric acid through adenine nucleotide degradation. In addition, alcoholic drinking made from diverse materials contains various proportions of purines [72]. Studies have confirmed that alcohol consumption could increase the risk of hyperuricemia and gout, no matter what type of alcoholic beverages individuals consumed with different levels of alcohol [73,74]. SUA levels increased with the quantity of alcohol intake, and this increase was more obvious in individuals who drank beer or distilled alcoholic beverages [75]. Ethanol intake of 55 g/day could cause a significantly increased risk of hyperuricemia [76]. At the same time, daily drinkers had a nearly five-fold increase in the incidence associated with hyperuricemia compared to non-drinkers [73]. If individual is also accompanied with obese, the sum of the incorporated risk of excessive obesity plus alcohol intake was greater than the risk of hyperuricemia caused by obesity alone, as demonstrated in one data studying the connection between obesity, alcohol consumption and hyperuricemia from the Chinese National Health Survey from 2012-2017 [77]. Also, daily alcohol drinking is independently linked with SUA levels and the risk of chronic kidney diseases (CKD), non-drinkers with the highest SUA levels having a higher risk of CKD in a prospective cohort study [78]. Researches have also elucidated that alcohol intake was intensely linked with an increased risk of gout [73,75,79]. Compared with non-alcohol drinker, those who drank more than 15 g each day had the 93% increased risk of gout [31]. Therefore, limiting alcohol consumption makes sense to decrease the risk of hyperuricemia and gout. Based on the current findings, decreasing the risk of hyperuricemia by limiting the intake of alcoholic beverages is important, and furthermore, individuals suffered from hyperuricemia should limit all kinds of alcohol consumption to decrease the risk of recurrence.

4.2. Some foods intake decreases the risk of hyperuricemia

4.2.1. Dairy products

Dairy products are popular natural sources of rich nutrients with high contents of protein and contain a variety of probiotics. Probiotics are beneficial to the human body in a variety of ways, which can promote intestinal motility and body digestion, enrich the intestinal flora in the body, and even have a profitable effect on the prevention/treatment of obesity, diabetes, hypertension and cardiovascular disease [80]. Drinking milk can lower SUA levels mainly because milk proteins are thought to facilitate the excretion of uric acid [81]. Based on the determination of purine content in different dairy products by Kaneko et al. (2014), purines are virtually absent from dairy products (<50 mg/100 g). Increasing dairy product consumption in daily diet, such as cheese, low-fat milk, and low-fat yogurt could reduce the risk of

hyperuricemia [82]. Dairy products contain two distillates, glucomegapeptide and G600 milk fat extract, which possess anti-inflammatory impacts in patients with gout, and this anti-inflammatory property might help reduce gout risk through inhibiting the inflammatory reaction produced by sodium urate crystals that accumulates at the joints. Also, skim milk powder containing G600 milk fat extract may lower the frequency of gout damages [83]. In addition, milk-forming proteins such as whey protein and casein have the effects of reducing uric acid, which might elucidate the opposite connection between dairy intake and uric acid levels [58]. Two selected strains, *lacticaseibacillus rhamnosus* 1155 and *limosilactobacillus fermentum* 2644, had the ability to reduce uric acid, and dairy products containing these strains could be used as a new tactic to stabilize SUA levels [84]. What's more, avoiding milk intake or other dairy products intake because milk allergy could increase the risk of hyperuricemia [85].

4.2.2. Vegetables

Vegetables contain a variety of bioactive functional compounds, for example, polyphenols, carotenoids, dietary fiber, flavonoids, ascorbic acid, and a variety of different proportions of micro and macro nutrients. In addition, vegetables are also an abundant source of minerals and vitamins with antioxidant, anti-cancer, antibacterial and anti-inflammatory properties, and play a vital role in human life. Intaking more vegetables is related with an inferior occurrence of diseases such as gastrointestinal disease, heart disease, stroke, neurodegenerative ailments, hyperuricemia, diabetes and cancer [86]. Compared with animal-based (meat and seafood intake) dietary types, plant-based dietary types are negatively correlated with SUA concentration. Purine-rich vegetables consumption is not related with the occurrence of hyperuricemia and low vegetable consumption may cause hyperuricemia [22]. Dietary polyphenols are divided into phenolic acids, stilbenes, lignans, curcuminoids, flavonoids, and chalcones. As a potential anti-hyperuricemia dietary factor, dietary polyphenols can inhibit uric acid production by inhibiting the activity of xanthine oxidase, improve intestinal uric acid secretion, increase renal uric acid secretion and inhibit uric acid reabsorption [49]. Also, intaking vegetables that contain more vitamin C is helpful for asymptomatic hyperuricemia [87]. Individuals who eat vegetables less than 3 times per week were about 1.9 times more possible to cause hyperuricemia than those ate vegetables more than 3 times each week [88]. Kanbara et al. (2012) claimed that excretion of uric acid (37.0 vs 25.9 mg/dL) and SUA levels (4.3 vs 4.9 mg/dL) among Japanese college students in a high vegetable alkaline diet compared to an acidic diet that contained many animal products. The possible mechanism might be that vegetables are alkaline foods with low-fat. Increasing vegetables intake could alkalinize the urine with the increased solubility of uric acid and accelerate uric acid excretion. Based on current researches, adequate vegetable intake is crucial to reduce the risk of hyperuricemia.

4.2.3. Dietary fiber and micronutrient-rich foods

Dietary fiber derives mainly from coarse grains and other plants and consist of complex non-starchy carbohydrates and lignin, which cannot be digested in the small intestine and need to access to the colon and to be fermented by bacteria. The metabolites produced by bacterial fermentation are then used by humans to

meet their energy needs [89]. In addition, dietary fiber is subdivided into polysaccharides (comprising non-starch polysaccharides, resistant oligosaccharides, and resistant starch), or is present in the forms of insoluble and soluble in foods [90]. Increasing fiber intake can increase satiety, inhibit fat absorption, maintain intestinal health, and be beneficial for some gastrointestinal diseases. Dietary fiber promotes intestinal movement and the excretion of uric acid in the gut, and it can also help diabetics lower blood pressure and accelerate cholesterol excretion [42,89]. Micronutrients (including vitamins and minerals) are critical for the maintenance of life and normal physiological functions. Micronutrient deficiencies are common worldwide, and pregnant women, infant, and kids are most at risk. In resource-poor regions and countries, consumption of vegetables, fruits and grain is the most economical and sustainable way to reduce micronutrient deficiencies. Inadequate intake of essential micronutrients can lead to nutrition-related diseases. Clinical researches have proved that dietary fiber consumption had a helpful impact on reducing the risk of hyperuricemia, and the consistency and volume of dietary fiber can hinder purine absorption in the human digestive system [91,92]. One nationally representative data assessed the connection between dietary fiber consumption and SUA levels and the possibility of occurrence on hyperuricemia among 66,427 Chinese adults, and suggested that total fiber or cereal fiber intake were negative correlated with the levels of SUA and the incidence of hyperuricemia [84]. It was also recommended to increase the intake of vitamins A, B1, B2 and B6, and dietary calcium, potassium, magnesium and zinc to prevent the incidence of gout in adults [93]. In addition, study has shown that dietary vitamin E consumption was negatively correlated with hyperuricemia, particularly for man and participants aged more than 60 years [94]. In brief, consuming foods rich in dietary fiber and micronutrients, such as fruits, vegetables, grains and legumes, is vital to reduce the risk of hyperuricemia.

4.2.4. Foods are rich in unsaturated fatty acids

Fatty acids are the primary components of lipids, which can be divided into SFAs and UFAs. Polyunsaturated fatty acids (PUFAs) are dominating ingredients of cell membranes and important nutrients in the treatment of NAFLD, autoimmune reactions and chronic diseases. Among these, omega-3 and omega-6 fatty acids are identified as important fatty acids as they cannot be produced in the body and must be ingested through diet [95]. A diet with high UFAs was concerned with a lower SUA levels and promoted insulin resistance, which may be beneficial for relieving symptoms in hyperuricemic patients accompanied with NAFLD [96]. SUA levels could be reduced by consuming 2 g fish oil each day for 8 weeks [97]. Besides, Stea et al. (2016) reported that a daily consumption of 700 mg omega-3 fatty acid supplements for 3 months decreased SUA levels among healthy older males in an intervention study. In patients with CKD, the higher intake of fatty acid, including monounsaturated fatty acid (MUFA) and PUFAs, was relevant to a lower risk of hyperuricemia [98]. Therefore, consuming foods rich in unsaturated fatty acid, such as marine fish oils, nut, flax and chia seeds, is useful to reduce the risk of hyperuricemia.

4.2.5. Unsweetened tea and coffee

Tea and coffee are a very important part of human beverage consumption. Consuming a certain amount of unsweetened tea and coffee has been shown to have a variety of health benefits. Caffeine, the main component of coffee, has been shown to competitively inhibit xanthine oxidase activity in rats, thereby reducing serum urate concentration. In addition, the phenolic chlorogenic acid found in coffee acts as a strong antioxidant, which can improve insulin sensitivity and play a role in alleviating symptoms in patients with hyperuricemia associated with metabolic syndrome [99]. Tea polyphenols, a compound contained in tea, can help relieve symptoms of hyperuricemic patients. Polyphenols such as catechins, gallic acid and theaflavins in tea play a key role in preventing the occurrence of hyperuricemia with animal model studies, by inhibiting xanthine oxidase activity in the liver during uric acid production, increasing uric acid transporter expression, and thus reducing uric acid production or increasing uric acid excretion [99-101]. Although different types of tea differ in their chemical composition and function, regardless of the type of tea, drinking 600-800 mL of tea daily (about 5 g dry weight tea) may be beneficial for asymptomatic hyperuricemia patients [100].

4.3. Food restriction and hyperuricemia

4.3.1. Fruits

Fruits contain bioactive nutritional molecules (carbohydrates, vitamins, minerals, dietary fiber, etc.) and non-nutritional phytochemicals (polyphenols, flavonoids, carotenoids, saponins, bioactive peptides, etc.), which are of great benefit to human health and a very important part of diet [102]. Clinical researches have proved that superfluous fructose intake can increase SUA levels and cause hyperuricemia. Fruits contain a certain amount of fructose and a small number of purines, and the product of fructose and purine metabolism is uric acid. However, due to the numerous components in fruits, their effect on SUA is complex [103]. Some fruits, such as blueberry, have a high fructose content which may increase the concentration of SUA, but are rich in compounds and nutrients that can lower SUA levels, such as vitamin C, polyphenols, dietary fiber, and micronutrient that are believed to be offset by a combination [104]. The mechanisms of these components affecting the concentration of SUA could be summarized as following: suppressing the activity of xanthine oxidase, lowering uric acid reabsorption and promoting uric acid excretion [105]. Red dragon fruit is rich in flavonoids and has potential anti-hyperuricemia effects [106]. Although SSBs are the largest supplier for total fructose intaking, fruits and their products are also an important contributor. The free fructose contents in different fruits are shown in Table 1. As can be known from the Table 1, jujube has the highest fructose content (20.62 g/100g), followed by plum (12.45 g/100g) and grapes (10.00 g/100g). The fructose content of peach, nectarine, plum, pineapple, and durian is relatively low (< 2 mg/kg). No free fructose is detected in persimmon and kiwi fruit. Appropriate fruit intake could postpone or restrain the incidence of hyperuricemia and may reduce the complications caused by hyperuricemia [31,82]. Dietary Guidelines for Americans 2020-2025 suggest that a healthy dietary pattern requires restricting calories derive from added sugars and sugars in food to lower than 10% of daily dietary calories. According to the 2022 Dietary Guidelines for Chinese residents, high fruit intake is defined as fruit intake ≥350 g each day.

However, a normal amount consumption level of fructose-containing sugar intake can not increase SUA levels or the risk of hypertension. Berries are known for their antioxidant and anti-aging properties. Cherries, cranberries and other berries have also been proved to have anti-hyperuricemic abilities [107]. Anthocyanins are the main bioactive components of blueberries, cranberries and cherries, and they have antioxidant and anti-inflammatory abilities, which reduced SUA levels, as well as the ability to downregulate NFkB-mediated osteoclastogenesis [108]. Therefore, individuals should select fruits with a low fructose content, such as peach, plum, durian, melon, pineapple and orange, in order to decrease the risk of hyperuricemia. Cranberries, strawberry, blueberries, berry fruits, and various types of cherry fruits are the potential substitutes of complementary therapies for hyperuricemia.

Table 1. The free fructose content in different fruits.

Fruits	Free fructose content (g/100g)	Reference
Jujube	20.62	http://www.ars.usda.gov/nutrientdata
Grapes	10.00	[109]
Blueberry	9.02	http://www.ars.usda.gov/nutrientdata
Apple	8.40	http://www.ars.usda.gov/nutrientdata
Lemon	7.90	http://www.ars.usda.gov/nutrientdata
Lychee	7.60	[109]
Pear	6.76	http://www.ars.usda.gov/nutrientdata
Banana	6.09	http://www.ars.usda.gov/nutrientdata
Blackberry	5.10	[109]
Kiwifruit	4.35	http://www.ars.usda.gov/nutrientdata
Raspberry	3.40	[109]
Mango	3.10	[109]
Strawberry	2.84	http://www.ars.usda.gov/nutrientdata
Dragon fruit	2.80	[109]
Cherry	2.40	[109]
Melon	2.40	http://www.ars.usda.gov/nutrientdata
Orange	2.36	http://www.ars.usda.gov/nutrientdata
Grapefruit	2.30	[109]
Pineapple	1.90	[109]
Durian	1.60	[109]
Plum	1.60	[109]
Peach	1.53	[109]
Nectarine	1.39	[109]

4.3.2. Legumes

Legumes, especially soy foods, provide abundant quality protein and favorable fatty acid configuration. However, soy products provide a moderate and high purine load in the legumes group, and thus given the potential for uric acid production, restricted intake is necessary [60]. Besides, some legumes (such as soybeans) contain a high oxalate content (ranging from 0.67 to 3.5 g/100 g dry weight). After oxalic acid is absorbed by the body, it cannot be excreted through kidney metabolism, which combines with calcium to form insoluble salt and further precipitates to form kidney stones, thus interfering uric acid excretion [110]. The key is to replace a high purine content of beans with a low to moderate purine content of beans, such as replacing soybeans with non-soy beans. One study showed that soy food consumption was negatively associated with hyperuricemia in middle-aged Chinese man [23]. Liu et al. reported that more soy food consumption (6.1 g/d vs 0.5 g/d) would be related to a lower presence of hyperuricemia in women after

regulating for confounding factors [111]. However, Dalbeth et al. claimed that soy intake (80 g/d) led to an increase in SUA concentration of approximately 10% [112]. Therefore, appropriate intake of legumes is necessary to prevent the occurrence of hyperuricemia. According to the determination of purine content in foods by Kaneko et al. [60], soy-based foods contained certain amounts of purines (100–3000 mg/kg), and the purine contents of fermented soybean freeze-dried tofu and dried-soybean were 1,139 mg/kg, 2,931 mg/kg and 1,725 mg/kg, respectively, while some legumes were low in purines (500 mg/kg), such as almond, broad bean, green-peas and peanut. The purine content of soy milk depends on the purine content of the beans used. Soy milk has a higher purine content with 220 mg/kg than milk (0 mg/kg), so it is recommended that hyperuricemic patients consume milk instead of soymilk [113]. According to the current researches, it is recommended to intake legumes with a low purine content, such as almond, broad bean, green-peas and peanut, and moderate intake of legumes with a higher content of purines, such as soybeans, to decrease the risk of hyperuricemia.

5. Individualized diet for the population with complications of hyperuricemia

As patients with hyperuricemia may be accompanied by some complications, personalized diet should be emphasized for patients with hyperuricemia accompanied with different metabolic diseases such as metabolic syndromes, CKD, CVD, NAFLD, and other diseases.

Metabolic syndrome (MS) is closely associated with hyperuricemia and gout, and it is a group of metabolic disorders mainly characterized by abdominal obesity, hyperglycemia, hypertension, and dyslipidemia. Insulin resistance, an important feature of metabolic syndrome, reduces urate excretion by the kidneys [114-115]. The pathogenesis of MS is relatively complex and patients are at high risk of diabetes and cardiovascular diseases [114]. Increased expression of uric acid transporter 1 (URAT1) and glucose transporter 9 (GLUT9), as well as insulin resistance induced glycolysis disorder, may be linked with the occurrence of hyperuricemia in metabolic syndrome [21]. Besides, fructose induced hyperuricemia, which causes endothelial dysfunction (reduced endothelial NO levels) and insulin resistance, may be a novel pathogenesis of metabolic syndrome [116]. Dietary recommendations for patients with hyperuricemia and metabolic syndrome are to reduce the intake of foods with high fructose content and increase the intake of low-fat dairy products and dietary fiber.

Meanwhile, hyperuricemia can cause or accelerate the progression of CKD by activating NLRP3 inflammatories that promote the secretion of active interleukin (IL-1β) and IL-18 inflammatory cytokines from inflammatory cells, and induces epithelial interstitial transformation and vascular endothelial injury, leading to kidney damage [117]. Study has shown that people with hyperuricemia on a vegan diet had fewer uric acid crystals in their urine and a 31% lower risk of developing CKD, partly due to the consumption of vegetables rich in antioxidants such as vitamins A, C, and E, carotenoids, phenolic acids, and flavonoids. Secondly, most vegetables are rich in dietary fiber which can improve the intestinal microbiome of patients with CKD to reduce oxidative stress and inflammation, promote endothelial health, and prevent the occurrence of CKD or slow the progression of CKD [118]. For hyperuricemia patients with CKD, plant-based

foods such as fruits, vegetables, nuts, and whole grains are the priority, while animal-derived foods should can be consumed in small amounts to prevent nutrient loss.

CVD is one of the most common complications of hyperuricemia. Hyperuricemic patients accompanied with CVD are encouraged to embrace dietary polyphenols rich in plant-based diet, which can improve the release of nitric oxide in endothelial cells, activate cyclovir monophosphate in vascular smooth muscle cells, and relax blood vessels. In addition, dietary polyphenols may act either directly on vascular smooth muscle cells to relax blood vessels by activating BK channels or inhibiting calcium channels to exert vascular elasticity, or indirectly on vascular smooth muscle cells to relax blood vessels by activating potassium channels in endothelial cells through Ca^{2+}, leading to hyperpolarization of Ca^{2+} and inhibiting Ca^{2+} inflow into vascular smooth muscle cells [119,120]. Clinical studies have shown that the consumption of bioactive derivatives of plant foods, including dietary flavonoids, soybean peptides, oligosaccharides, vitamins and unsaturated fatty acids, had a protective effect on cardiovascular disease [121,122]. Dietary recommendations for patients with hyperuricemia accompanied by cardiovascular diseases are to increase the intake of vitamin C and other micronutrients, unsaturated fatty acids.

As a potential manifestation of hyperuricemia, decreased insulin clearance caused by hepatocyte steatosis in patients with NAFLD can lead to insulin resistance, which can increase uric acid production, reduce uric acid excretion. Besides, insulin significantly increased URAT1 and decreased ABCG2 levels, leading to an increased UA reabsorption finally resulting in the occurrence of hyperuricemia [123]. It is recommended to increase unsaturated fatty acids intake, and reduce added sugar intake (especially fructose) in patients with hyperuricemia associated with NAFLD.

6. Conclusions

High intake of dietary purines is known to increase SUA levels and could cause hyperuricemia. Uric acid transporters play an important role in the process of purine metabolism and could be used as a basic target for clinical treatment of hyperuricemia. Maintaining SUA levels within a certain range (serum urate is less than 420 μmol/L in males and 360 μmol/L in females) is the key to prevent the occurrence of hyperuricemia. Although exogenous purine intake accounts for a small proportion, as a factor that individuals can control and regulate initiatively, diet plays a crucial role on the risk of hyperuricemia. This review provides a comprehensive summary about the effect of dietary types associated with hyperuricemia, including beneficial, adverse and some restrictive dietary factors on the risk of hyperuricemia are explored. The conclusion can be summarized as following:

(1) Some dietary factor intake, such as purine, fructose and alcohol, could increase the risk of hyperuricemia. However, water, unsaturated fatty acids, vitamin C and some micronutrients (such as folic acid, vitamin D, dietary magnesium, zine and iron, polyphenols and saponins) could decrease the risk of hyperuricemia.

(2) Modification of foods intake for the prevention of hyperuricemia is suggested as following: limiting the intake of animal meats, animal organs, and seafoods which contain high purine contents; reducing

sugar-sweetened and alcohol beverages consumption and replacing them with unsweetened tea and coffee; encouraging the consumption of vegetables, dairy products (especially low-fat dairy products), foods rich in unsaturated fatty acid, as well as foods rich in dietary fiber and micronutrients.

(3) Consumption of fruits and legumes in moderation is useful. Low-fructose of fruits is recommended, such as peach, plum, durian, pineapple and orange. Various kinds of cherry fruits are the potential substitutes for hyperuricemia complementary therapy. In addition, individuals are also recommended to intake legumes with a low purine content, such as almond, broad bean, green-peas and peanut to reduce the risk of hyperuricemia.

(4) Dietary recommendations for hyperuricemic patients accompanied with metabolic syndrome are to reduce the intake of foods with high fructose content and increase the intake of low-fat dairy products and dietary fiber. For hyperuricemia patients with CKD, plant-based foods such as fruits, vegetables, nuts, and whole grains are the priority, but animal-derived foods such as white meat can also be consumed in small amounts to prevent nutrient loss. It is recommended to increase the intake of vitamin C and other micronutrients, unsaturated fatty acids, and reduce added sugars intake in patients with NAFLD or CVD combined with hyperuricemia.

7. Challenges and future perspectives

The current clinical researches have a short observation period and a limited study population on the effect of diet on hyperuricemia, and thus long-term follow-up and long-term intervention studies on a wider range of population would be needed in the future after some complex factors are eliminated. More importantly, since the composition of food is often complex, it is necessary to explore the comprehensive mechanism and definite action targets of bioactive compounds in food to reduce the occurrence of hyperuricemia. In addition, more reasonable dietary suggestions without nutritional loss in human body need further consideration for individuals with different hyperuricemia complications in the future.

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