Indian Journal of Fundamental and Applied Life Sciences ISSN: 2231– 6345 (Online)
An Online International Journal Available at http://www.cibtech.org/jls.htm
2023 Vol. 13, pp. 14-26/Shanthi et al.
Review Article (Open Access)

NUTRITIONAL STRATEGIES FOR MANAGING HYPERURICEMIA AND GOUT: A COMPREHENSIVE REVIEW FROM DIVERSE STUDIES

***Shanthi Lakshmi Duraimani, Bhawna Sati, Krishna R, Abinaya Selvanathan, Swetha Dharmaraj, Ishita Lote**
Answergenomics Pvt Ltd, New Delhi, India
**Author of Correspondence: shanthilakshmi.cd@gmail.com*

ABSTRACT
Hyperuricemia and gout are prevalent metabolic disorders characterized by elevated serum uric acid levels, which can lead to painful and debilitating joint inflammation.
A comprehensive review has been conducted to formulate up-to-date nutritional recommendations for managing Gout and Hyperuricemia. Studies have consistently shown that purine-rich foods, such as organ meats, red meat, and seafood, contribute to higher serum uric acid levels, while low-purine foods, including vegetables, fruits, and low-fat dairy products, are associated with reduced uric acid concentrations. Dairy products, particularly low-fat variants, have been found to aid uric acid excretion and lower gout risk. Fructose and sugar-sweetened beverages have been identified as significant contributors to hyperuricemia, while coffee consumption, particularly decaffeinated, and higher vitamin C intake show potential protective effects against elevated serum uric acid levels. Notably, tart cherries have emerged as a potential dietary addition to reduce serum uric acid levels and attenuate gout flares, with their anti-inflammatory properties contributing to their beneficial effects. In conclusion, a personalized approach, including a balanced diet rich in plant-based foods, limited purine-rich, and sugary items, and appropriate intake of low-fat dairy products, may effectively manage hyperuricemia and reduce the risk of gout.

Keywords: *Hyperuricemia, gout, dietary factors, purine-rich foods, low-purine foods, dairy products, fructose, sugar-sweetened beverages, coffee, vitamin C, tart cherries, personalised approach, balanced diet, anti-inflammatory properties*

INTRODUCTION

Hyperuricemia is a metabolic disorder characterised by elevated uric acid levels in the blood. Uric acid is a natural waste product that forms when the body breaks down purines, which are substances found in certain foods and tissues. Usually, uric acid dissolves in the blood and passes through the kidneys, where it is excreted in the urine. When the amount of purines in our body goes beyond what is considered normal, it can disrupt the process of producing and getting rid of uric acid. As a result, uric acid levels in our bloodstream increase (Jin *et al.*, 2012).

Elevated serum uric acid (SUA) levels can pose a risk for several other conditions when not effectively managed. These include:

1. **Kidney Stones:** Solid uric acid formations that can develop within the kidneys.
2. **Hypertension:** Elevated blood pressure levels.
3. **Cardiovascular Disease:** A condition characterized by the heart's diminished ability to pump blood efficiently.
4. **Stroke:** A sudden interruption of blood flow to the brain.
5. **Diabetes:** A chronic disorder involving improper insulin production or utilization.
6. **Chronic Kidney Disease:** A gradual decline in kidney function over time.
7. **Gout**. (Tien *et al.,* 2022)

Gout, a form of arthritis, occurs when uric acid crystals accumulate in the joints, causing inflammation, severe pain, and other symptoms. Typically affecting the lower extremity joints, particularly the big toe, gout can also impact other joints in the body. It has historically been referred to as the "disease of kings" due to its association with opulent diets, but it is now understood that various factors, including genetics and lifestyle, contribute to its development.

It is also important to note that gout affects only a portion of hyperuricemia patients, with approximately 36% being susceptible to developing this condition. Furthermore, it's important to note that not all individuals with gout exhibit hyperuricemia, and in fact, up to 76% of asymptomatic hyperuricemia patients do not show deposition of Mono Sodium Urate (MSU) crystals.

Hyperuricemia and gout can have a significant impact on quality of life, as gout attacks can be debilitating and recurrent. The management of hyperuricemia and gout involves a combination of pharmacological interventions, lifestyle modifications, and dietary changes. Dietary modifications play a crucial role in reducing uric acid levels and preventing gout attacks. By adopting a balanced and tailored diet, individuals with hyperuricemia and gout can better manage their condition, reduce symptoms, and improve long-term outcomes (Ragab, Elshahaly, and ardin 2017)

Understanding the underlying mechanisms and exploring evidence-based nutritional recommendations is essential in providing effective management strategies for individuals with hyperuricemia and gout. Addressing the root causes and implementing appropriate dietary interventions can alleviate symptoms, prevent gout attacks, and improve the overall quality of life for those affected by these conditions. In this comprehensive review, our objective was to explore the mechanism of uric acid and evidence-based nutritional recommendations to mitigate the effects of hyperuricemia and GOUT.

The Production of Uric Acid: A Closer Look

Uric acid is a complex organic compound found in our bodies. It is produced from two types of purine nucleic acids called adenine and guanine, with the help of various enzymes. The process involves several steps: adenosine monophosphate (AMP) is converted to inosine, and Guanosine monophosphate (GMP) is converted to guanosine. These nucleosides are further transformed into hypoxanthine and guanine, respectively. Hypoxanthine is then oxidized to xanthine, which is finally converted into uric acid. Uric acid exists mainly as urate in our body, and when its concentration increases, it can form crystals called monosodium urate (MSU) [Figure 1]. Humans cannot convert uric acid into a more soluble compound called allantoin due to the absence of a specific enzyme called uricase. Normally, the kidneys help eliminate uric acid from our bodies daily (Maiuolo *et al.,* 2016). Table 1 shows the normal reference value of uric acid among men and women (Zhang *et al.,* 2022).

Under normal circumstances, about 90% of the uric acid produced in our body is reabsorbed, and the remaining 10% is eliminated through urine and faeces. However, when there is an excessive intake or production of purines, the balance between uric acid synthesis and excretion is disrupted, leading to elevated uric acid levels in the bloodstream. Most of the purines in our body come from the food we eat, while the rest are made by our cells. Our body has a coordinated process to break down and recycle purines, turning them into uric acid. This process mainly happens in the liver and small intestine. The kidneys play a significant role in removing approximately two-thirds of the circulating uric acid. At the same time, the remaining one-third is excreted through the intestines with the help of the gut microbiota (Desideri *et al.,* 2014).

Dietary Factors Influencing Hyperuricemia and Gout

A. *Purine-rich foods:* Kaneko *et al.,* 2020 determined the total purine content and purine base in around 80 different food products and classified them into various groups based on their purine levels. The classification included five groups: very low (<50 mg/100 g), low (50-100 mg/100 g), moderate (100-200 mg/100 g), high (200-300 mg/100 g), and very high (>300 mg/100 g) purine content [See Table 2]. However, it should be noted that dried food was not classified as high or very high purine, despite potentially high apparent values, due to the moisture evaporation during the drying process (Kaneko *et al.,* 2020).

Dairy products, known for their minimal purine content, have been reported to aid in the excretion of uric acid and reduce SUA levels. Consequently, dietary intake of dairy products is recommended in guidelines for individuals with hyperuricemia and gout, including those from Europe, America, and Japan (Jordan *et al.,* 2007; Khanna *et al.,* 2012; Yamanaka and Japanese Society of Gout and Nucleic Acid Metabolism 2011). The purine content of various cereals, beans, and seeds was examined in this study.

However, it is important to consider serving sizes. For instance, one serving (2.5 g) of Chinese soup stock contained only 12.7 mg of purine, and dried yeast, with a serving size of approximately 1g, had about 8.5mg of purine. (Determination of total purine and purine base content of 80 food products to aid nutritional therapy for gout and hyperuricemia) (H. K. Choi *et al.,* 2004).

The above study results were aligned with many independent intervention studies. For instance, a prospective study conducted over 12 years aimed to examine the association between dietary factors and the development of gout. The study involved 47,150 men without a history of gout at the beginning. The results revealed that higher consumption of meat and seafood was associated with an increased risk of gout, indicated by a higher relative risk. Conversely, a higher intake of dairy products was associated with a decreased risk of gout. Consuming purine-rich vegetables and total protein intake did not show an increased risk of gout (Choi, Liu, and Curhan 2005).

Choi *et al.,* 2005 examined the relationship between dietary factors and SUA levels in a representative sample of adults in the US. The study analysed data from 14,809 participants and assessed the intake of purine-rich foods, protein, and dairy products using a food-frequency questionnaire. The results showed that a higher intake of total meat and seafood was associated with increased SUA levels, while a higher intake of dairy products was associated with decreased levels. Adjustments for various factors confirmed these associations. Total protein intake did not have a significant impact on SUA levels. Additionally, individuals who consumed milk or yogurt regularly had lower SUA levels than non-consumers. These findings also suggest that meat and seafood consumption may elevate uric acid levels, while dairy consumption may have a protective effect. Similarly, studies conducted by Teng *et al.,* 2015 and Mena-Sanchez *et al.,* 2020 also aligned with the above research findings. Hence, higher consumption of red meat, chicken, and sea foods increases hyperuricemia and GOUT, whereas consumption of vegetables, plant protein, and dairy lowers the risk of hyperuricemia.

B. Fructose and sugar-sweetened beverages: Fructose consumption in the human diet is increasing globally, mainly through sugars added to processed foods and drinks. High-fructose corn syrup (HFCS), derived from corn starch, is widely used in the United States as a low-cost sweetener. In Europe, sucrose is still the primary sweetener. However, the regulation of glucose and fructose syrup production in the European Union has changed, allowing for the growth of HFCS production. Fructose is commonly found in sugar-sweetened beverages (SSBs) and is strongly associated with obesity and related chronic diseases. The metabolism of fructose primarily occurs in the liver. The correlation between fructose intake, elevated SUA levels, and metabolic syndrome suggests a potential pathogenic role of fructose-induced hyperuricemia (Russo *et al.,* 2020).

Fructose, primarily absorbed by the intestinal Glut5 transporter, undergoes metabolic processes involving fructokinase and aldolase B. Fructose 1-phosphate is produced through fructokinase activity, leading to the depletion of intracellular phosphate and ATP, resulting in transient inhibition of protein synthesis. Adenosine monophosphate is generated and degraded by adenosine monophosphate deaminase, which leads to inosine monophosphate and uric acid synthesis. This process causes an increase in intracellular uric acid levels, leading to a temporary rise in circulating uric acid levels [Figure 2](Russo *et al.,* 2020).

Many observational studies have shown a significant increase in uric acid levels among people who consumed high sugar-sweetened beverages. For instance, a study conducted by Choi *et al.,* 2008 examined the relationship between the intake of sugar-sweetened soft drinks, diet soft drinks, and SUA levels. Data from a nationally representative sample of adults in the United States were analyzed. The results showed that increasing consumption of sugar-sweetened soft drinks was associated with higher SUA levels. Adjusting for covariates, individuals consuming different categories of sugar-sweetened soft drinks had higher SUA levels than those who did not consume them. The odds of having hyperuricemia also increased with higher consumption of sugar-sweetened soft drinks. However, the consumption of diet soft drinks was not associated with SUA levels or hyperuricemia (J. W. J. Choi *et al.,* 2008).

Another interesting study by Carran EL et al 2016 investigated the acute impact of consuming commercial sugar-sweetened soft drinks on plasma uric acid levels. Forty-one participants were randomized into a control group and an intervention group. The control group consumed glucose and fructose beverages, while the intervention group consumed soft drinks of varying volumes (355 ml and 600 ml). Blood samples were collected at baseline, 30 minutes, and 60 minutes after consumption, and plasma uric acid levels were analyzed. The results showed that 355 ml and 600 ml of soft drink consumption led to small and transient increases in plasma uric acid levels compared to the glucose control. These findings suggest that even small volumes of sucrose-sweetened soft drinks can cause short-term elevations in uric acid levels (Carran *et al.,* 2016).

Numerous other studies have corroborated the findings above. For instance, Carren *et al.*, (2016) conducted a randomized controlled trial, Siqueira *et al.*, (2021) undertook a longitudinal study, and Meneses-Leon *et al.*, (2020) conducted a longitudinal analysis of the health workers cohort study. All three investigations yielded consistent outcomes that the intake of sugar-sweetened soft drinks may contribute to elevated SUA levels and an increased risk of hyperuricemia, while diet soft drink consumption does not have the same effect (Bae, Chun *et al.,* 2014; Siqueira *et al.,* 2021; Meneses-León *et al.,* 2020).

C. *Dairy products on reducing GOUT and hyperuricemia:* A study aimed to examine the association between dairy product consumption and the risk of hyperuricemia in an elderly Mediterranean population with metabolic syndrome (MetS). The study analysed cross-sectional data from 6,329 individuals with overweight/obesity and MetS, using a food frequency questionnaire to assess their dairy consumption. Cox regression analyses evaluated the relationship between dairy product consumption quartiles and hyperuricemia prevalence. The results showed that participants in the highest quartile of total dairy product consumption, including low-fat dairy products, total milk, low-fat milk, low-fat yogurt, and cheese, had a lower prevalence of hyperuricemia. Specifically, their multi-adjusted prevalence ratios were significantly lower than the lowest quartile. Hence, a high intake of total dairy products, including low-fat dairy products, total milk, low-fat milk, low-fat yogurt, and cheese, was associated with a decreased risk of hyperuricemia in the elderly Mediterranean population with MetS (Mena-Sánchez *et al.,* 2020).

Cândido FG and his team performed a placebo-controlled trial aimed to investigate the relationship between calcium and the gout-protective effect of low-fat dairy products. Thirty-five low-calcium-consuming adult females were assigned to three treatment groups: low-calcium breakfast (control), high-calcium breakfast from calcium citrate, or high-calcium breakfast from skim milk. Despite no significant changes in body weight or fat, both calcium interventions significantly reduced serum urate and ionic calcium levels. Calcium supplementation, whether from dairy or calcium citrate, reduced serum urate concentrations, indicating that the urate-lowering effect of calcium contributes to the gout-protective effect of low-fat dairy consumption.

Another study investigated the association between the intake of selected food groups and beverages and SUA levels. The study utilized baseline data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), including 14,320 active and retired civil servants aged 35-74. The findings revealed that a higher intake of dairy products was associated with lower serum UA levels in both sexes, exhibiting a dose-response relationship. This study also revealed that high meat intake was linked to high UA levels in women, while organ meat consumption was associated with high UA levels in men. Fish, fruits, vegetables, and legume intake did not significantly correlate with serum UA. These findings also suggest a potential beneficial role of dairy products in regulating UA levels (Silva *et al.*, 2020).

D. *Role of tart cherry on reducing GOUT and hyperuricemia:* Tart cherries have gained increasing recognition in the realm nutrition due to their purported health benefits. The Prunus cerasus species, cultivated worldwide, has witnessed significant market growth in recent decades, attributable to advancements in agricultural practices and food processing technology. Distinguished by their polyphenol content, tart cherries exhibit a distinctive composition comprising anthocyanins, flavonols, and chlorogenic acids (Alba C, Daya, and Franck 2019).

A total of 10 healthy women participated in the study and consumed two servings of cherries after an overnight fast. Blood and urine samples were collected before consumption and at specific time intervals after consumption. The results showed that plasma urate levels decreased significantly 5 hours after cherry consumption compared to baseline levels. Urinary urate levels increased, reaching peak excretion at 3 hours post-consumption. Marginal decreases in plasma C-reactive protein (CRP) and nitric oxide (NO) concentrations were observed 3 hours post-consumption. Plasma albumin and tumor necrosis factor-alpha levels remained unchanged. The cherries' vitamin C content was present as dehydroascorbic acid, and increased plasma ascorbic acid indicated its bioavailability. The decrease in plasma urate levels supports the potential anti-gout efficacy of cherries. The slight reductions in inflammatory markers (CRP and NO)

suggest that cherry compounds may have inhibitory effects on inflammatory pathways, as observed in vitro (Jacob *et al.*, 2003).

Another study investigated the effects of tart cherry juice (TCJ) consumption on SUA levels of inflammation, lipid levels, and glycemia in overweight and obese individuals at risk of gout. In a randomized, placebo-controlled crossover study, participants consumed 240 mL (8 oz) of TCJ or a placebo beverage for four weeks, with a washout period in between and an additional four weeks of the alternate beverage. TCJ consumption led to a significant 19.2% reduction in SUA concentrations and showed potential reductions in proinflammatory markers. The findings suggest that TCJ may effectively mitigate hyperuricemia associated with gouty arthritis (Martin and Coles 2019).

Schlesinger and his team investigated the effectiveness of cherry juice concentrate in preventing gout flares. Three studies were conducted, comparing cherry juice concentrate to pomegranate juice concentrate, evaluating the long-term use of cherry juice concentrate, and studying its impact on interleukin secretion in vitro. The results showed that consuming cherry juice concentrate reduced the incidence of flares in gout patients, with an even more significant reduction when combined with urate-lowering therapy (ULT). There was no significant change in serum urate levels, indicating that the decrease in flares was likely due to the anti-inflammatory properties of cherry juice concentrate. The study also found that cherry juice concentrate inhibited the secretion of IL-1β. These findings also suggest that consuming cherry juice concentrate for an extended period may help reduce acute gout flares through its anti-inflammatory actions.

E. *Soy and its controversies about Hyperuricemia and GOUT:* The impact of soy products on uric acid levels is controversial among nutritionists. While some earlier information suggested that soy might increase uric acid, recent studies have provided evidence to the contrary, indicating that soy does not significantly raise uric acid levels.

For instance, a meta-analysis and systematic review included 17 studies to investigate the impact of soy consumption on plasma uric acid levels. These studies comprised three human clinical trials focusing on acute effects, five long-term human studies with ten data sets, and nine animal trials with 29 data sets. The diverse range of studies allowed for a comprehensive evaluation of the relationship between soy and uric acid levels, highlighting the contrasting effects of soy and its products on SUA concentrations (Duan *et al.*, 2022).

Another study aimed to investigate the long-term effects of soy intake on SUA levels among 450 postmenopausal women with prehypertension or prediabetes. Two randomized controlled trials were conducted, one with soy protein and the other with whole soy, and the participants were divided into combined soy foods, combined isoflavone, and placebo groups. After six months, the combined soy foods group showed a lower decrease in UA levels than the other groups. The net reduction in UA was 14.5 μmol/L (4.9% decrease) in the combined soy foods group compared to the placebo group. Soy intake did not increase urate levels in Chinese postmenopausal women with prehypertension or prediabetes (Liu *et al.*, 2015).

These two meta-analyses and systematic reviews provide compelling evidence that soy intake does not increase uric acid levels and can be considered a safe and beneficial protein source for individuals with hyperuricemia or gout. Nutritionists and healthcare professionals should reconsider their perspectives and consider incorporating soy and its products, such as tofu, bean curd cake, and dried bean curd sticks, into the dietary recommendations for these patients, as it may offer potential health benefits without adversely affecting uric acid levels.

F. *Different diets that can impact hyperuricemia and GOUT:* Different diets can impact hyperuricemia and gout. Zhou *et al.*, 2022, conducted a nutritional epidemiological survey in China to investigate the association between dietary patterns, blood uric acid concentrations, and hyperuricemia. The findings revealed that a plant-based nutritional pattern was negatively correlated with blood uric acid levels, indicating that higher adherence to a plant-based diet was associated with lower uric acid

concentrations. Conversely, an animal-based dietary pattern showed a positive correlation with blood uric acid levels, suggesting that increased consumption of animal-based foods was associated with higher uric acid concentrations. Additionally, the study highlighted that a dietary pattern characterized by a high intake of poultry, sugary beverages, and animal organs, along with a low intake of desserts and snacks, was linked to a significantly higher risk of hyperuricemia. However, it should be noted that the study did not provide specific details regarding the types of desserts and snacks associated with a lack of impact on uric acid levels (Zhou *et al.*, 2022).

In another study by Chio Yokose *et al.*, in 2020, the impact of weight loss diets on serum urate (SU) levels and cardiometabolic risk factors in individuals with moderate obesity was investigated. Three weight-loss diets were assessed: low-fat, restricted-calorie; Mediterranean, restricted-calorie; and low-carbohydrate, non-restricted-calorie diets. Results showed that all three diets significantly reduced SU levels at 6 and 24 months for all participants, with no notable differences between the diet groups. Additionally, improvements were observed in various cardiometabolic risk factors, indicating that nonpurine-focused weight loss diets can simultaneously benefit SU levels and cardiovascular health. Notably, participants with hyperuricemia experienced even more significant SU reductions, highlighting the potential benefits for those at risk of gout. The findings suggest that weight loss diets, regardless of their specific composition, can effectively lower SU levels, likely through reduced adiposity and insulin resistance associated with weight loss.

Another study found that adherence to a Mediterranean diet is associated with lower SUA levels and a reduced likelihood of hyperuricemia. The research included 2380 participants without cardiovascular or renal disease. Using the MedDietScore, the study observed an inverse relationship between adherence to the Mediterranean diet and SUA levels, independent of factors like sex, overweight, hypertension, glucose metabolism, alcohol, and coffee intake. Specifically, those with higher MedDietScores had significantly lower uric acid levels and a 70% lower likelihood of hyperuricemia than those with lower scores (Kontogianni *et al.*, 2012).

Moreover, another study investigated the relationship between a vegetarian diet and the risk of gout, independent of hyperuricemia, in two Taiwanese cohorts. Results revealed that vegetarians had lower uric acid concentrations than nonvegetarians. Moreover, Taiwanese vegetarians exhibited a significantly reduced risk of gout compared to nonvegetarians in both cohorts. The risk reduction was 60% in Cohort 1 and 39% in Cohort 2. Importantly, this protective association persisted even after adjusting for baseline hyperuricemia in Cohort 1. Adopting a vegetarian diet may confer a lower risk of gout in the Taiwanese population by targeting multiple pathways involved in gout pathogenesis, including uric acid reduction and anti-inflammation. These results highlight the potential benefits of plant-based diets in mitigating gout and its associated cardiometabolic comorbidities (Chiu *et al.*, 2020).

The study aimed to compare the effects of Dietary Approaches to Stop Hypertension (DASH)-style diets with different macronutrient proportions on serum urate reduction. The secondary analysis was conducted on a randomized trial of adults with prehypertension or hypertension, who were given three DASH-style diets in random order for six weeks each. The diets emphasized different macronutrient proportions: a carbohydrate-rich (CARB) diet, a protein-rich (PROT) diet with approximately half of the protein from plant sources, and an unsaturated fat-rich (UNSAT) diet. The results showed that only the PROT diet significantly reduced serum urate levels at the end of the 6-week feeding period, compared to baseline. Neither the CARB nor the UNSAT diet showed significant reductions in serum urate. Additionally, the PROT diet was found to be more effective in lowering serum urate compared to both CARB and UNSAT diets. The findings suggest that a DASH-style diet emphasizing plant-based protein may have a beneficial effect on reducing serum urate levels (Belanger *et al.*, 2021). These comprehensive studies collectively indicate that nutritionists and health professionals should reconsider incorporating good-quality proteins like soy and plant-based diets as dietary recommendations for individuals with hyperuricemia and gout.

G. *Vitamin C and hyperuricemia/GOUT:* Higher vitamin C intake is associated with lower SUA concentrations in a population-based analysis of 1,387 men without hypertension and BMI <30 kg/m². The inverse relationship was observed up to a vitamin C intake of 400-500 mg/d, beyond which the effect plateaued. This suggests that vitamin C may be preventive in managing hyperuricemia and gout, supporting its potential importance in dietary strategies for at-risk individuals. The associations remained consistent even when using dietary data assessed several years before blood collection, reinforcing the significance of vitamin C intake in maintaining healthy uric acid levels (Gao *et al.*, 2008).

In a cross-sectional analysis of 9400 participants, dietary vitamin C intake significantly differed between hyperuricemic and non-hyperuricemic subjects in both males and females. The risk of hyperuricemia decreased with increasing dietary vitamin C intake in both genders after adjusting for various factors. Total vitamin C intake also showed an effect on hyperuricemia risk in females (Bae, Shin, *et al.*, 2014).

Pooled data from three National Health and Nutrition Examination Survey cycles showed that higher total vitamin C and dietary vitamin C intake were associated with a lower risk of hyperuricemia in the general US adult population. Participants with higher vitamin C intake had significantly reduced odds of hyperuricemia, with the inverse association observed in both men and women, regardless of adjustments for covariates (Sun *et al.*, 2018). A meta-analysis of 13 randomised controlled trials (RCTs) assessing the effect of vitamin C supplementation on SUA levels revealed a significant reduction in SUA levels by -0.35 mg/dl. The trials involved 556 participants, with a median dosage of 500 mg/day of vitamin C and a median study duration of 30 days. Placebo-controlled trials showed more significant reductions in uric acid, indicating that vitamin C supplementation can effectively lower SUA levels (Juraschek, Miller, and Gelber 2011). These collective findings emphasize the potential benefits of vitamin C in managing hyperuricemia and GOUT, making it a valuable dietary component for individuals at risk of these conditions.

H. *Coffee and tea consumption:* Higher coffee intake was associated with a reduced risk of hyperuricemia among American women with low serum ferritin levels, but this protective effect was not observed among women with high serum ferritin levels, indicating a potential modifying effect of serum ferritin on the association between coffee intake and hyperuricemia (Agoons *et al.*, 2021).

Higher coffee intake was associated with lower SUA levels in a nationally representative sample of US adults. Participants consuming 4 to 5 cups or 6 cups or more of coffee daily had significantly lower SUA levels than non-coffee consumers. Decaffeinated coffee also showed a modest inverse association with SUA levels, and higher coffee consumption was associated with a lower frequency of hyperuricemia. However, total caffeine intake from coffee, other beverages, and tea did not significantly affect SUA levels (H. K. Choi and Curhan 2007).

In contrast, a cross-sectional analysis of the general Korean population found no significant difference in SUA levels between non-coffee drinkers and different coffee consumption groups (i.e., <1 cup, 1-2 cups, 2-5 cups, and ≥5 cups) in both men and women. The study concludes that no significant relationship exists between coffee consumption and SUA levels in the general Korean population (Jung *et al.*, 2020).

Using Mendelian randomization analysis in a Japanese population, habitual coffee consumption was significantly and inversely associated with gout risk. Individuals with higher coffee intake had a lower risk of developing gout, independent of SUA levels. This suggests that coffee may have other beneficial mechanisms in reducing gout risk beyond its impact on uric acid levels (Shirai *et al.*, 2022).

These diverse findings highlight the complex relationship between coffee intake and hyperuricemia or gout risk, indicating the need for further research to elucidate the underlying mechanisms and potential modifiers involved in these associations.

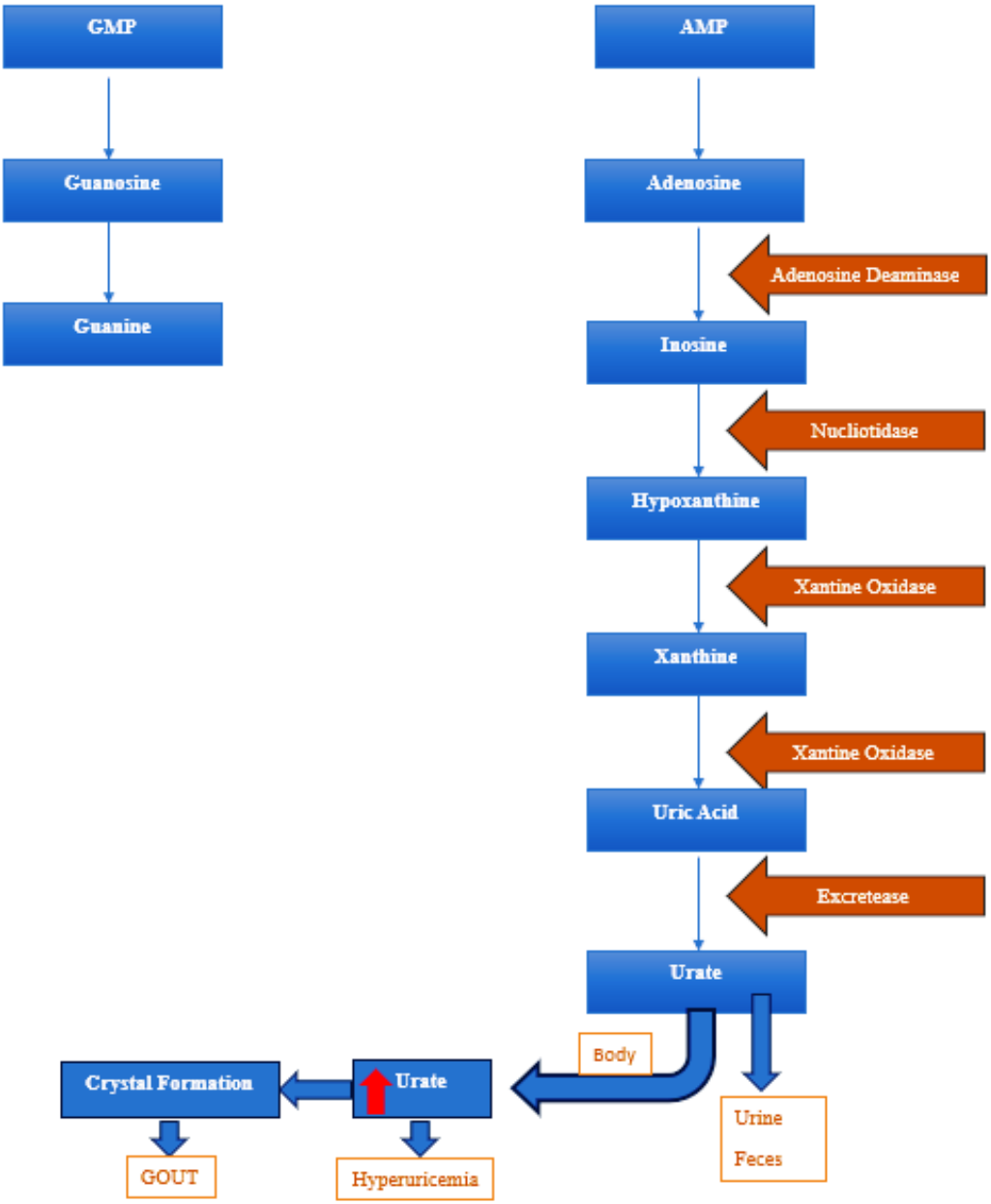

Figure 1: Uric Acid Metabolism

I. *Omega-3 fatty acids:* Low omega-3 fatty acids are associated with frequent gout attacks, likely due to their anti-inflammatory effects and inhibition of inflammation pathways triggered by monosodium urate crystals, the primary cause of gout attacks. Supplementation with omega-3 fatty acids may be beneficial in preventing acute gout attacks. However, studies have limitations, including self-reported gout attack frequency and inadequate information on other dietary factors influencing gout (Abhishek, Valdes, and Doherty 2016).

A 6-month pilot clinical trial explored the effects of omega-3 fish oil supplementation on serum urate, weight, and BMI in individuals with gout. Although no significant difference in serum urate levels or BMI was observed between the fish oil and control groups, higher red cell omega-3 concentrations correlated with fewer gout flares. This suggests a potential role for omega-3 supplements as prophylaxis against gout flares when initiating urate-lowering therapy, but further well-powered clinical trials are needed. It should

be noted that some participants experienced gastrointestinal adverse effects from the supplementation (M. Zhang *et al.*, 2019).

These findings underscore the potential benefits of omega-3 fatty acids in managing gout attacks, offering a promising avenue for further investigation and optimizing dietary interventions for gout patients.

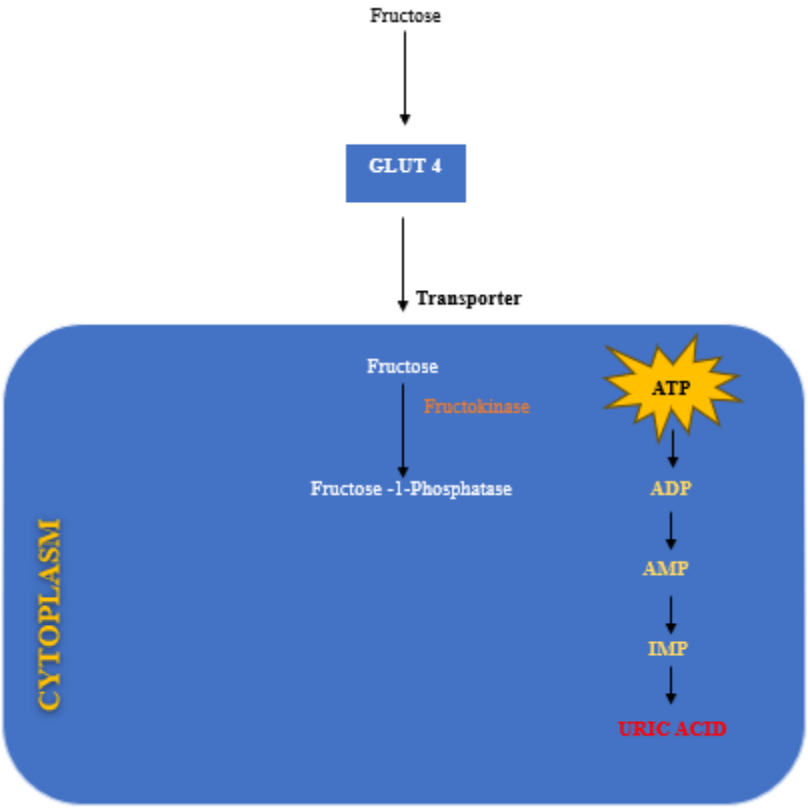

Figure 2: Fructose Induced Uric Acid Production

Table 1: Normal Range for Serum Uric Acid

NORMAL RANGE (MG/DL)		
ADULT MALE	**Adult Female**	
	Pre-Menopausal	**Post - Menopausal**
3.5 AND 7.2 MG/D	2.6 and 6.0 mg/dL	3.5 and 7.2 mg/dL

Table 2: Categorization of Very Low Purine Content Foods and Very High Purine Content Foods

Very Low Purine Content (< 50 mg/100)	**Very High Purine Content (> 300 mg/100)**
Garbanzo Bens	Chicken Liver
Noodles	Cutlass Fish
Red Peas	Anchovies
Walnuts	Chicken Soup Stock
Green Pepper	Dried Chinese Soup Sock
Tomato	Dried Yeast
Radish	
Lettuce	

J. *Gut microbiome in reducing uric acid levels:* In the context of a meta-analytical investigation, the administration of probiotics has demonstrated a discernible capacity to mitigate SUA concentrations. This empirical observation emerged from a comprehensive scrutiny encompassing four distinct randomized controlled trials (RCTs), collectively encompassing a cohort of 294 participants (Zeng *et al.,* 2022). In the context of a randomized, double-blind, and placebo-controlled clinical investigation, a cohort of 25 individuals diagnosed with hyperuricaemia and/or gout was subjected to a dietary intervention involving the supplementation of Lactobacillus gasseri yogurt. Notably, the culmination of this 8-week trial witnessed a marked reduction in their SUA levels. An imbalance in purine levels, such as from eating too many purine-rich foods, can lead to excess uric acid in our bloodstream (Yamanaka *et al.*, 2019).

CONCLUSION

Based on the inferences from various studies on hyperuricemia and gout, the following nutritional recommendations can be made to help manage and prevent these conditions:

1. **Limit Purine-Rich Foods:** Reduce consumption of purine-rich foods such as organ meats, red meat, and seafood. Instead, focus on a diet rich in low-purine foods like vegetables, fruits, and whole grains. Incorporate plant-based proteins and legumes such as soya beans as an alternative to meat.
2. **Increase Dairy Intake**: Include low-fat dairy products in the diet, as they have been associated with reduced SUA levels and a lower risk of gout. Consuming milk, yogurt, and cheese may aid in the excretion of uric acid.
3. **Reduce Fructose and Sugar-Sweetened Beverages:** Limit the intake of fructose and sugar-sweetened beverages, as they have been linked to increased uric acid levels. Choose water, herbal teas, or unsweetened beverages as alternatives.
4. **Incorporate Tart Cherries:** Tart cherries have shown potential benefits in reducing SUA levels and mitigating gout flares. Consider including tart cherry juice or fresh cherries as part of the diet.
5. **Personalized Dietary Approach:** Tailor dietary recommendations to individual factors such as genetic predisposition, lifestyle, and comorbidities. A personalized approach may optimize uric acid regulation and gout prevention.
6. **Consider Omega-3 Supplementation:** Omega-3 fatty acids may have anti-inflammatory effects and could be beneficial in managing gout attacks. Consult a healthcare professional before starting any supplements.

To summarise, adopting a balanced and individualized dietary approach that emphasizes plant-based foods, limits purine-rich and sugary items, and includes low-fat dairy products can effectively manage hyperuricemia and reduce the risk of gout. However, it is essential to consult with a healthcare provider or a registered dietitian before making significant dietary changes to ensure a safe and appropriate approach based on individual health needs and conditions.

ACKNOWLEDGMENTS

We are grateful to all the researchers whose valuable contributions have enriched this review. Their insights, expertise, and dedication have greatly enhanced the quality and scope of this work.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this manuscript. The research was conducted in an unbiased manner, and the content of the review is solely based on the scientific findings presented in the included studies. The authors have no financial, professional, or personal relationships that could have influenced the objectivity of the research or the interpretation of its results.

REFERENCES

Abhishek, A., Valdes, A. M., & Doherty, M. (2016). Low omega-3 fatty acid levels associate with frequent gout attacks: a case-control study. *Annals of the Rheumatic Diseases,* **75**(4), 784-785.

Agoons, D. D., Agoons, B. B., Kaze, A. D., & Komanduri, S. (2021). Effect of Serum Ferritin on the Association Between Coffee Intake and Hyperuricemia Among American Women: The National Health and Nutrition Examination Survey. *Cureus,* **13**(3), e13855.

Bae, J., Chun, B. Y., Park, P. S., Choi, B. Y., Kim, M. K., Shin, M. H., Lee, Y. H., Shin, D. H., & Kim, S. K. (2014). Higher consumption of sugar-sweetened soft drinks increases the risk of hyperuricemia in the Korean population: The Korean Multi-Rural Communities Cohort Study. *Semin Arthritis Rheum,* **43**(5), 654-661.

Bae, J., Shin, D. H., Chun, B. Y., Choi, B. By., Kim, M. K., Shin, M. H., Lee, Y. H., Park, P. S., & Kim, S. K. (2014). The effect of vitamin C intake on the risk of hyperuricemia and serum uric acid level in Korean Multi-Rural Communities Cohort. *Joint Bone Spine,* **81**(6), 513-519.

Belanger, M. J., Wee, C. C., Mukamal, K. J., Miller III, E. R., Sacks, F. M., Appel, L. J., Shmerling, R. H., Choi, H. K., & Juraschek, S. P. (2021). Effects of dietary macronutrients on serum urate: results from the OmniHeart trial. *The American Journal of Clinical Nutrition,* **113**(6), 1593-1599.

Cândido, F. G., Alves, R. D. M., Freitas, D. M. D. O., Bittencourt, J. M., Rocha, D. M. U. P., & Alfenas, R. D. C. G. (2022). Urate-lowering effect of calcium supplementation: Analyses of a randomized controlled trial. *Randomized Controlled Trial,* **49**, 86-91.

Carran, E. L., White, S. J., Reynolds, A. N., Haszard, J. J., & Venn, B. J. (2016). Acute effect of fructose intake from sugar-sweetened beverages on plasma uric acid: a randomized controlled trial. *Eur J Clin Nutr,* **70**(9), 1034-1038.

Chio Yokose, Natalie McCormick, Sharan K Rai, Na Lu, Gary Curhan, Dan Schwarzfuchs, Iris Shai, Hyon K Choi. (2020). Effects of Low-Fat, Mediterranean, or Low-Carbohydrate Weight Loss Diets on Serum Urate and Cardiometabolic Risk Factors: A Secondary Analysis of the Dietary Intervention Randomized Controlled Trial (DIRECT). *Diabetes Care,* **43**(11), 2812-2820.

Chiu, T. H. T., Liu, C.-H., Chang, C.-C., Lin, M.-N., & Lin, C.-L. (2020). Vegetarian diet and risk of gout in two separate prospective cohort studies. *Clinical Nutrition,* **39**(3), 837-844.

Choi, H. K., & Curhan, G. (2007). Coffee, tea, and caffeine consumption and serum uric acid level: the third national health and nutrition examination survey. *Arthritis & Rheumatism,* **57**(5), 816-821.

Choi, H. K., Atkinson, K., Karlson, E. W., Willett, W., & Curhan, G. (2004). Purine-Rich Foods, Dairy, Protein Intake, and the Risk of Gout in Men. *New England Journal of Medicine,* **350**, 1093-1103.

Choi, H. K., Liu, S., & Curhan, G. (2005). Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum,* **52**(1), 283-289.

Choi, J. W. J., Ford, E. S., Gao, X., & Choi, H. K. (2008). Sugar-sweetened soft drinks, diet soft drinks, and serum uric acid level: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum,* **59**(1), 109-116.

da Silva, M. T., Diniz, M. F. H. S., Coelho, C. G., Vidigal, P. G., Telles, R. W., & Barreto, S. M. (2019). Intake of selected foods and beverages and serum uric acid levels in adults: ELSA-Brasil (2008-2010). *Public Health Nutrition,* **23**(3), 506-514.

Desideri, G., Castaldo, G., Lombardi, A., Mussap, M., Testa, A., Pontremoli, R., Punzi, L., & Borghi, C. (2014). Is it time to revise the normal range of serum uric acid levels? European Review for Medical and Pharmacological Sciences, **18**(9), 1295-1306.

Doe, J. J. (2012). Uric Acid, Hyperuricemia, and Vascular Diseases. Frontiers in Bioscience, 17, 656-669.

Duan Y, Qi Q, Liu Z, Zhang M, Liu H. Soy consumption and serum uric acid levels: A systematic review and meta-analysis. *Frontiers in Nutrition, 9*, 975718.

Gao, X., Curhan, G., Forman, J. P., Ascherio, A., & Choi, H. K. (2008). Vitamin C Intake and Serum Uric Acid Concentration in Men. *Journal of Rheumatology,* **35**(9), 1853–1858.

Jacob, R. A., Spinozzi, G. M., Simon, V. A., Kelley, D. S., Prior, R. L., Hess-Pierce, B., & Kader, A. A. (2003). Consumption of cherries lowers plasma urate in healthy women. *The Journal of Nutrition,* **133**(6), 1826-1829.

Johnson, C. D., Smith, A. B., Doe, J., Luo, J. J., Wang, H., Yin, Y., & Yang, X. F. (2022). To Treat or Not to Treat? Effect of Urate-Lowering Therapy on Renal Function, Blood Pressure and Safety in Patients with Asymptomatic Hyperuricemia: A Systematic Review and Network Meta-Analysis. Journal of the American Board of Family Medicine, **35**(1), 140-151.

Jordan, K. M., Cameron, J. S., Snaith, M., Zhang, W., Doherty, M., Seckl, J., Hingorani, A., Jaques, R., Nuki, G., on behalf of the British Society for Rheumatology and British Health Professionals in Rheumatology Standards, Guidelines and Audit Working Group (SGAWG) (2007). British Society for

Rheumatology and British Health Professionals in Rheumatology Guideline for the Management of Gout. Rheumatology, **46**(8), 1372–1374.
Jung, J. H., Seok, H., Choi, S. J., Kim, C., Bang, C. H., & Song, G. G. (2020). Relationship between coffee consumption and serum uric acid level in the general Korean population: A nationwide cross-sectional study. *International Journal of Rheumatic Diseases,* **23**(3), 420-427.
Juraschek, S. P., Miller, E. R., 3rd, & Gelber, A. C. (2011). Effect of oral vitamin C supplementation on serum uric acid: a meta-analysis of randomized controlled trials. *Arthritis Care & Research (Hoboken),* **63**(9), 1295-1306.
Kaneko, K., Takayanagi, F., Fukuuchi, T., Yamaoka, N., Yasuda, M., Mawatari, K., & Fujimori, S. (2020). Determination of total purine and purine base content of 80 food products to aid nutritional therapy for gout and hyperuricemia. Nucleosides, Nucleotides & Nucleic Acids, **39**(10-12), 1449-1457.
Khanna, D., Khanna, P. P., Fitzgerald, J. D., Singh, M. K., Bae, S., Neogi, T., Pillinger, M. H., Merill, J., Lee, S., Prakash, S., Kaldas, M., Gogia, M., Perez-Ruiz, F., Taylor, W., Lioté, F., Choi, H., Singh, J. A., Dalbeth, N., Kaplan, S., Niyyar, V., Jones, D., Yarows, S. A., Roessler, B., Kerr, G., King, C., Levy, G., Furst, D. E., Edwards, N. L., Mandell, B., Schumacher, H. R., Robbins, M., Wenger, N., & Terkeltaub, R. (2012). 2012 American College of Rheumatology guidelines for management of gout. Part 2: Therapy and antiinflammatory prophylaxis of acute gouty arthritis. Arthritis Care and Research, **64**(10), 1447-1461.
Kontogianni, M. D., Chrysohoou, C., Panagiotakos, D. B., Tsetsekou, E., Zeimbekis, A., Pitsavos, C., & Stefanadis, C. (2012). Adherence to the Mediterranean diet and serum uric acid: the ATTICA study. *Scandinavian Journal of Rheumatology,* **41**(6), 442-449.
Liu ZM, Ho CS, Chen YM, Woo J. Can soy intake affect serum uric acid level? Pooled analysis from two 6-month randomized controlled trials among Chinese postmenopausal women with prediabetes or prehypertension. *European Journal of Nutrition,* **54**(1), 51-8.
Maiuolo, J., Oppedisano, F., Gratteri, S., Muscoli, C., & Mollace, V. (2016). Regulation of uric acid metabolism and excretion. International Journal of Cardiology, 213, 8-14.
Martin, K. R., & Coles, K. M. (2019). Consumption of 100% Tart Cherry Juice Reduces Serum Urate in Overweight and Obese Adults—Current *Developments in Nutrition,* **3**(5), nzz011.
Mayo Clinic (2021). Gout - Symptoms and Causes. Rochester, MN: Mayo Clinic. Available from: [https://www.mayoclinic.org/diseases-conditions/gout/symptoms-causes/syc-20372897]
Mayta-Apaza, A. C., Marasini, D., & Carbonero, F. (2019). Tart Cherries and health: Current knowledge and need for a better understanding of the fate of phytochemicals in the human gastrointestinal tract. *Critical Reviews in Food Science and Nutrition,* **59**(4), 626-638.
Mena-Sánchez, G., Babio, N., Becerra-Tomás, N., Martínez-González, M. Á., Díaz-López, A., Corella, D., ... Salas-Salvadó, J. (2020). Association between dairy product consumption and hyperuricemia in an elderly population with metabolic syndrome. *Nutr Metab Cardiovasc Dis,* **30**(2), 214-222.
Mena-Sánchez, G., Babio, N., Becerra-Tomás, N., Martínez-González, M. Á., Díaz-López, A., Corella, D., Zomeño, M. D., Romaguera, D., Vioque, J., Alonso-Gómez, Á. M., Wärnberg, J., Martínez, J. A., Serra-Majem, L., Estruch, R., Bernal, R., Lapetra, J., Pintó, X., Tur, J. A., Lopez-Miranda, J., Cano-Ibáñez, N., Gaforio, J. J., Matía-Martín, P., Daimiel, L., Llisterri Caro, J. L., Vidal, J., Vázquez, C., Ros, E., Garcia Arellano, A., Palau, A., Fernández-Carrión, R., Pérez-Vega, K. A., Morey, M., García de la Hera, M., Vaquero-Luna, J., Carmona-González, F. J., Abete, I., Álvarez-Pérez, J., Casas, R., Fernández-García, J. C., Santos-Lozano, J. M., Corbella, E., Sureda, A., Ruiz-Canela, M., Barragán, R., Goday, A., Martín, M., Altozano Rodado, M. C., Toledo, E., Fitó, M., & Salas-Salvadó, J. (2020). Association between dairy product consumption and hyperuricemia in an elderly population with metabolic syndrome. *Nutrition, Metabolism and Cardiovascular Diseases,* **30**(2), 214-222.
Meneses-León, J., León-Maldonado, L., Macías, N., Torres-Ibarra, L., Hernández-López, R., Rivera-Paredez, B., ... Salmerón, J. (2020). Sugar-sweetened beverage consumption and risk of hyperuricemia: a longitudinal analysis of the Health Workers Cohort Study participants in Mexico. *American Journal of Clinical Nutrition,* **112**(3), 652-660.

Ragab, G., Elshahaly, M., & Bardinc, T. (2017). Gout: An old disease in a new perspective – A review. Journal of Advanced Research, **8**(5), 495–511.
Russo, E., Leoncini, G., Esposito, P., Garibotto, G., Pontremoli, R., & Viazzi, F. (2020). Fructose and Uric Acid: Major Mediators of Cardiovascular Disease Risk Starting at Pediatric Age. *Int J Mol Sci,* **21**(12), 4479.
Schlesinger, N., Rabinowitz, R., & Schlesinger, M. (2012). Pilot Studies of Cherry Juice Concentrate for Gout Flare Prophylaxis. *Journal of Arthritis,* **1**(1).
Shirai Y, Nakayama A, Kawamura Y, Toyoda Y, Nakatochi M, Shimizu S, Shinomiya N, Okada Y, Matsuo H, and Japan Gout Genomics Consortium (Japan Gout). Coffee Consumption Reduces Gout Risk Independently of Serum Uric Acid Levels: Mendelian Randomization Analyses Across Ancestry Populations. *ACR Open Rheumatol*, **4**(6), 534–539. Published online **2022** Mar 29.
Siqueira, J. H., Pereira, T. S. S., Velasquez-Melendez, G., Barreto, S. M., Benseñor, I. M., Mill, J. G., & Molina, M. C. B. (2021). Sugar-sweetened soft drinks consumption and risk of hyperuricemia: Results of the ELSA-Brasil study. *Nutr Metab Cardiovasc Dis,* **31**(7), 2004-2013.
Sun, Y., Sun, J., Wang, J., Gao, T., Zhang, H., & Ma, A. (2018). Association between vitamin C intake and risk of hyperuricemia in US adults. *Asia Pacific Journal of Clinical Nutrition, 27*(6), 1271-1276.
Teng, G. G., Pan, A., Yuan, J. M., & Koh, W. P. (2015). Food Sources of Protein and Risk of Incident Gout in the Singapore Chinese Health Study. *Arthritis Rheumatol, 67*(7), 1933–1942.
Yamanaka, H. (2011). Japanese Guideline for the Management of Hyperuricemia and Gout: Second Edition. Nucleosides, Nucleotides & Nucleic Acids, **30**(12), 1018-1029.
Yamanaka, H., Taniguchi, A., Tsuboi, H., Kano, H., & Asami, Y. (2019). Hypouricaemic effects of yogurt containing Lactobacillus gasseri PA-3 in patients with hyperuricaemia and gout: A randomised, double-blind, placebo-controlled study. Modern Rheumatology, **29**(1), 146-150.
Zeng, L., Deng, Y., He, Q., Yang, K., Li, J., Xiang, W., Liu, H., Zhu, X., & Chen, H. (2022). Safety and efficacy of probiotic supplementation in 8 types of inflammatory arthritis: A systematic review and meta-analysis of 34 randomized controlled trials. *Frontiers in Immunology,* **13**, 961325.
Zhang MA, Zhang Y, Terkeltaub R, Chen C, Neogi T. Effect of Dietary and Supplemental Omega-3 Polyunsaturated Fatty Acids on Risk of Recurrent Gout Flares. *Arthritis Rheumatol*, **71**(9), 1580-1586.
Zhang, Y., Chen, S., Yuan, M., Xu, Y., & Xu, H. (2022). Gout and Diet: A Comprehensive Review of Mechanisms and Management. Nutrients, 14(17), 3525.
Zhou, M., Huang, X., Li, R., Zhang, Z., Zhang, L., Gao, X., Yang, H., & Ma, Y. (2022). Association of dietary patterns with blood uric acid concentration and hyperuricemia in northern Chinese adults. *Nutrition Journal,* **21**(1), 42.