USDA and ODS-NIH Database for the Purine Content of Foods

Release 2.0

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List of Abbreviations:

Abbreviation	Definition
ATP	Adenosine triphosphate
CTSI-SECIM	Clinical and Translational Science Institute Southeast Center for Integrated Metabolomics
DASH	Dietary Approaches to Stop Hypertension
DNA	Deoxyribonucleic acid
DQES	Data Quality Evaluation System
DS	Dietary supplement
DSLD	Dietary Supplement Label Database
FDC	FoodData Central
FF	Foundation Foods
GTP	Guanosine-5'-triphosphate
HILIC-HRMS/MS	Hydrophilic Interaction Liquid Chromatography coupled with Tandem High Resolution-Mass Spectrometry
LOD	Limit of detection
MAFCL	Methods and Application of Food Composition Laboratory
NFNAP	National Food and Nutrient Analysis Program
NHANES	National Health and Nutrition Examination Survey
NIH-ODS	National Institutes of Health Office of Dietary Supplements
QC	Quality control
RNA	Ribonucleic acid
SEM	Standard error of the mean
SU	Serum urate
TTU	Texas Tech University
UF	University of Florida
USDA	United States Department of Agriculture
WWEIA	What We Eat in America

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A. Introduction: Purines in Health and Disease

Metabolism and Physiological Function of Purines in Humans

Purines are a class of nitrogenous compounds essential to all living organisms. Chemically, purines are heterocyclic aromatic organic compounds featuring a pyrimidine ring fused to an imidazole ring. Adenine, guanine, hypoxanthine, and xanthine are the primary purine bases in plants and animals (**Figure 1**). In foods, purines exist as free bases, nucleosides, nucleotides, and nucleic acids in RNA and DNA, with nucleic acids being the predominant form (Inazawa et al., 2014).

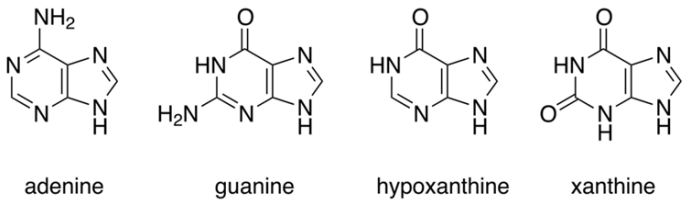

Figure 1. Chemical structures of four major purines

In the human body, purines are synthesized through the *de novo* synthetic pathway from the degradation of nucleic acids in live and dying cells. They are also obtained exogenously by consuming foods, beverages, and dietary supplements (DS) (Nelson & Voruganti, 2021; Ridi & Tallima, 2017). After ingestion, free purines are efficiently absorbed, mainly in the duodenum and jejunum of the small intestine. The metabolic pathways of purines in humans are summarized in **Figure 2.** Purines, related chemically to each other and absorbed from the diet, are metabolized differently (**Figure 2**) (Clifford et al., 1976; Brulé et al., 1992) and can be utilized through salvage pathways or can be catabolized into uric acid. In humans, uric acid is the final product of both endogenous and exogenous purine metabolism, with approximately 70% excreted by the kidneys and 30% through the intestines.

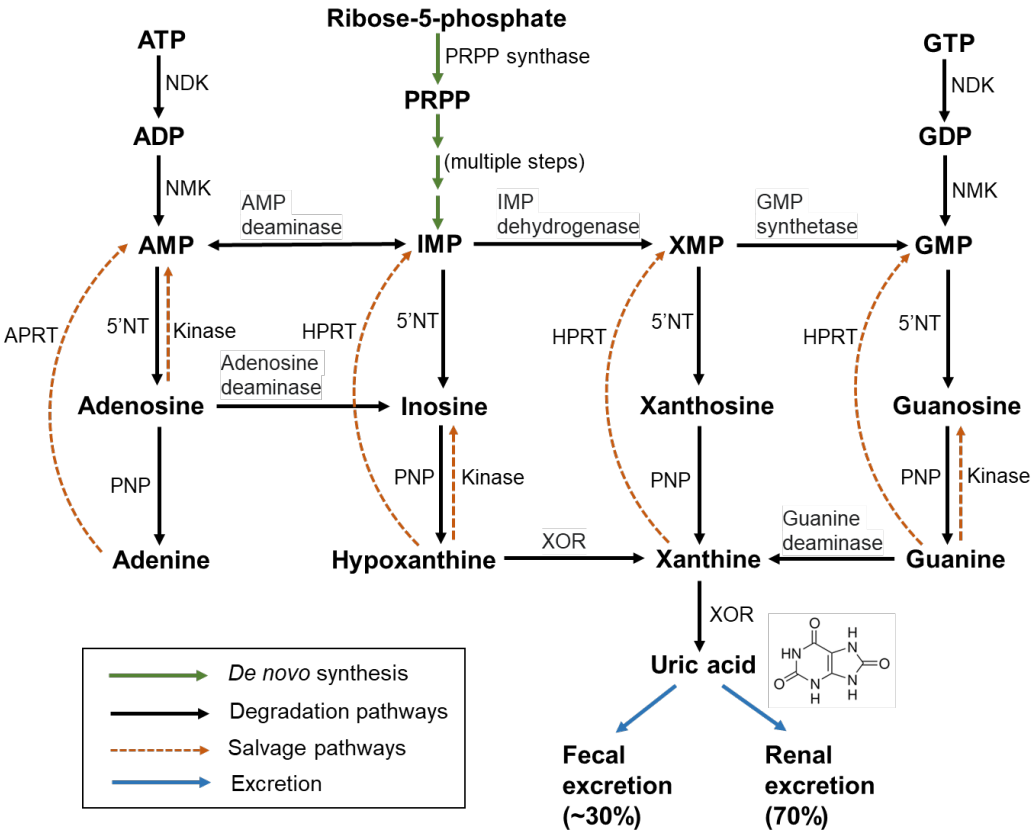

Figure 2. Metabolic pathways of purines and urate production in the human body (Abbreviations: ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; GDP, guanosine diphosphate; GMP, guanosine monophosphate; GTP, guanosine triphosphate; PRPP, phosphoribosyl pyrophosphate; IMP, inosine monophosphate; XMP, xanthosine monophosphate; NDK, nucleoside diphosphate kinase; NMK, nucleoside monophosphate kinase; 5'NT, 5'nucleotidase; APRT, adenine phosphoribosyl transferase; HPRT, hypoxanthine-guanine phosphoribosyl transferase; PNP, purine nucleotide phosphorylase; XOR, xanthine oxidoreductase)

Purines have many important biochemical functions including acting as metabolic signals within and between cells, providing energy, and regulating enzymatic activity (Nelson & Voruganti, 2021). Two purines, adenine and guanine, form nucleotides (such as ATP and GTP) which are components of the nucleic acids DNA and RNA (Kaneko et al., 2020; Nelson & Voruganti, 2021). Purine nucleosides such as adenosine and inosine in the body are key molecules controlling intracellular energy homoeostasis and nucleotide synthesis (Kaneko et al., 2020). Besides acting as chemical messengers, these purines act as endogenous ligands that bind to and activate plasmalemmal purinoceptors, which mediate extracellular communication that is sometimes referred to as "purinergic signaling" (Huang et al., 2021). Some purines serve specialized roles in the nervous system like guanosine and adenosine, which exert trophic effects following trauma (Rathbone et al., 1999; Jinnah et al., 2013). In addition, uric acid, the end metabolite of purines, is not simply a waste metabolic product, but also serves as an antioxidant for tissue repair, mediator of immune response, and in mitigating against neurological and autoimmune diseases (Nelson & Voruganti, 2021; Ridi & Tallima, 2017).

Hyperuricemia and Gout

Elevated serum urate (SU) levels (> 7 mg/dL in men and > 6 mg/dL in women) indicate the condition known as hyperuricemia. Hyperuricemia is a common disorder that affects patients of all ages and genders. Hyperuricemia prevalence rates in the United States are 20.2% in adult men and 20.0% in adult women, according to the National Health and Nutrition Examination Survey (NHANES) 2015-2016 (Chen-Xu et al., 2019). Hyperuricemia is caused by many factors, including lowered urate excretion and/or increased urate production through endogenous purine metabolism and/or dietary purine intake (Chittoor & Voruganti, 2020). Although hyperuricemic individuals are often asymptomatic and untreated, a causal relationship between hyperuricemia and the pathogenesis of a variety of other health problems has been proposed (Chittoor & Voruganti, 2020). It is associated with a higher risk of gout, hypertension, cardiovascular disease, and kidney disease (Chittoor & Voruganti, 2020).

Gout, a painful form of inflammatory arthritis caused by deposits of monosodium urate crystals in joints, occurs in about 25% of individuals with hyperuricemia. The presence of hyperuricemia and gout are worldwide health issues (Juraschek et al., 2021; Luk & Simkin, 2005). The gout disease burden grew globally from 1990 to 2017 due in concert with dietary and lifestyle changes, aging populations, and a rise in elevated body mass index. Gout is generally highest in developed regions and countries such as New Zealand, Australia, and the United States (Safiri et al., 2020; Xia et al., 2020). In recent years, Japan has experienced an annual increase in hyperuricemia and gout, possibly due to shifting dietary patterns; hyperuricemia prevalence affected 20-25% of Japanese adult males in 2010 while gout prevalence exceeded 1% in males aged 30 years and older (Hisatome et al., 2020). Recent modeling suggests the global burden of prevalent gout is expected to increase by more than 70% from 2020 to 2050 largely due to population growth and ageing (GBD 2021 Gout Collaborators, 2024). According to NHANES 2015-2016, nearly 4% of U.S. adults (9.2 million people) have gout, including 5.2% of men and 2.7% of women (Chen-Xu et al., 2019). The lower incidence of gout in women may be related to endocrine differences, where estrogen may inhibit the onset of arthritis and promote urate excretion (Hak et al., 2010; Luk & Simkin, 2005). Epidemiologic studies have linked dietary factors with gout risk (Chittoor & Voruganti, 2020; Nuki & Simkin 2006; Zhang et al., 2012). Traditionally, the causes of gout were attributed to an affluent or “western” lifestyle, including red meats, seafoods, and alcohol. Additional causes include obesity, ethnicity, biological sex, and genetics (Kuo et al., 2015; MacFarlane & Kim, 2014; Todd & Wright, 2020).

Accumulated evidence suggests that elevated SU levels may lead to a higher risk of cardiovascular disease, hypertension, dyslipidemia, obesity, metabolic syndrome, type 2 diabetes, and chronic renal disease (Vareldzis, Perez, & Reisin, 2024.). For example, it was observed that individuals with gout who also experienced a cardiovascular event were more likely to have had a recent gout flare than gout patients who did not have a cardiovascular event, suggesting that hyperuricemia and cardiovascular issues are closely related and that episodes of gout are linked to increased risk for cardiovascular events (Cipolletta et al., 2022). In addition, other potential underlying mechanisms may include regulating molecular signals, such as inflammatory response, oxidative stress, insulin resistance, endoplasmic reticulum stress, and endothelial dysfunction (Yanai et al., 2021).

Conventional treatment options for hyperuricemia as well as gout include exercise, weight loss if warranted, restriction of alcoholic and sugary beverages containing fructose, anti-inflammatory agents, and urate-lowering medications, as well as avoiding excessive meat and seafood intake (see section B

"Impact of Diet on Urate Levels") (Mallen et al., 2017; Richette & Bardin, 2017). Dietary modification is considered a primary preventive strategy to avoid gout flares (Nuki & Simkin, 2006; Chittoor & Voruganti, 2020; Todd & Wright, 2020).

B. Impact of Diet on Urate Levels

Dietary Factors and Urate Levels

Diet plays an integral role in hyperuricemia and gout via the contribution of dietary purines, leading to increased urate production as shown in observational and intervention studies. The traditional dietary approach to lowering urate levels is reducing the intake of high purine foods such as alcohol, meats, seafood, and some vegetables (MacFarlane & Kim, 2014; Nuki & Simkin, 2006; Rai et al., 2017). Frequent and high consumption of these foods and beverages are associated with elevated SU levels (Kaneko et al., 2014; Li et al., 2018; Villegas et al., 2012; Zgaga et al., 2012). A higher risk of hyperuricemia was observed with higher intake of red meat, poultry, seafood, and legumes in a large cross-sectional study of Chinese adults independent of sex, age, geographic region, body mass index, hypertension, consumption of refined grains, and alcohol intake (Aihemaitijiang et al., 2020). However, different cuts of meat and different types of seafood vary substantially in their total purine content, highlighting the importance of having purine data for specific foods to inform appropriate dietary choices instead of avoiding all meats and all seafood.

High purine vegetables are not associated with the risk of hyperuricemia or gout (Choi et al., 2004; Li et al., 2018; Villegas et al., 2012; Zgaga et al., 2012, Jakse et al., 2019). However, data on the purine content of various types of vegetables, such as different Brassicas (e.g., broccoli and cauliflower), are inconsistent and may lead to undue dietary restrictions. The data discussion section of this document, below, presents examples of this finding. Since various mechanisms affect hyperuricemia, restricting all purine-rich foods would unnecessarily eliminate certain foods that confer other health benefits. Therefore, these studies highlight the need for an accurate understanding of which food products, including DS, are high in purine content and increase the risk of hyperuricemia and gout.

Dietary factors besides total purine intake can impact urate levels, such as levels of specific uricogenic purine bases in foods. Uricogenic bases are purine bases that increase serum and urinary urate concentrations (Sarwar & Brulé, 1991). Hypoxanthine has shown the greatest dietary impact on increasing gout risk due to its effect on urate levels in the body (Clifford et al., 1976). Adenine also seems to increase urate levels (Clifford et al., 1976; Sarwar & Brulé, 1991; Brulé et al., 1992). The ratio of the four major purine bases (adenine, guanine, hypoxanthine, and xanthine) relative to total purines in a food seems influential in affecting SU, especially the impact of hypoxanthine (Kaneko et al., 2014).

Consuming dairy foods can decrease the risk of gout and hyperuricemia due to inverse associations with serum urate (Choi et al., 2004; Li et al., 2018; Zgaga et al., 2012). In one large observational study, low-fat dairy products were inversely associated with the incidence of gout (Choi et al., 2004). The protective effects of dairy have been attributed to the milk proteins casein and lactalbumin (Choi et al., 2005) and to the dairy fractions glycomacropeptide and G600 milk fat extract (Dalbeth et al., 2012). Soy food intake is also negatively associated with the risk of hyperuricemia and gout (Villegas et al., 2012; Li et al., 2018). High levels of meat and seafood consumption in the diet, but not total protein intake, have been linked to higher serum urate levels, while dairy intake has been inversely associated with serum urate levels (Choi et al., 2005).

Sugar-sweetened beverages are not sources of purines but should be avoided by those wishing to control urate levels because uric acid is produced by the breakdown of ATP through the metabolism of fructose (Luk & Simkin, 2005; Nelson & Voruganti, 2021). Sugar-sweetened beverages also appear to compete with urate excretion (Maiuolo et al., 2016; Chittoor & Voruganti, 2020).

Alcohol consumption has multiple mechanisms which raise SU (Pillinger & Keenan, 2008). The purine content of alcoholic beverages is only one of several factors involved in inducing changes to SU. Other factors include increased urate production and increased reabsorption of urate by the kidneys (Todd & Wright, 2020). Gout patients are typically advised to limit alcohol to one drink per day for women or two drinks per day for men (Khanna et al., 2012).

High doses of vitamin C (i.e., 400-500 mg/day) have beneficial effects on uric acid levels such as increased urinary urate excretion (Azzeh et al., 2017; Berger et al., 1977; Stein et al., 1976) and reduced SU concentration (Huang et al., 2005; Juraschek et al., 2011). In addition, vitamin C is highly associated with a reduced risk of gout (Choi et al., 2009). Vitamin C supplementation at 500 mg/day reduced SU and modestly reduced the incidence of new or recurrent gout diagnoses in middle-aged male physicians (Juraschek et al., 2022).

Weight loss is often recommended to gout patients since a lower body mass index has been associated with a lower risk of gout (Choi et al., 2005). However, reducing subjects' body mass indices led to either higher urate levels or no effects in a recent randomized clinical trial, and so additional studies are needed (Hu et al., 2021).

The effects of diet on urate levels differ by race, sex, body weight, and by the presence of certain genetic polymorphisms. For example, legume intake increased serum urate among African Americans compared to White adults, while alcohol intake increased serum urate to the same extent among African Americans and White adults in the United States (Beydoun et al., 2018). Dairy intake had an inverse effect on serum urate among African Americans but not White women (Beydoun et al., 2018). Recently, a cross-sectional analysis using NHANES 2011-2018 found that gout prevalence was twice as common among Asian adults in the United States than in any other race/ethnic groups (Yokose et al., 2023). In addition to diet, the higher prevalence of gout in Asian populations may be influenced by genetic polymorphisms (Butler et al., 2021).

Eating Patterns and Urate Levels

The Dietary Approaches to Stop Hypertension (DASH) diet, which focuses on fruit, vegetables, and low-fat dairy products, is being studied as a dietary intervention pattern for gout. Since nutrients and foods are consumed as part of a total diet, research on the effect of various eating patterns has presented an opportunity to examine the combinations of foods and micronutrients on hyperuricemia and gout risk (Rai et al., 2017).

The DASH diet is associated with lower gout risk among men (Rai et al., 2017) and lowered SU (Juraschek et al., 2016; Rai et al., 2017; Belanger et al., 2021). In a recent study, gout patients were instructed to follow the DASH diet along with other guidelines such as avoiding red meat, organ meat, shellfish, and excess alcohol consumption (Juraschek et al., 2021), presumably because those foods and beverages are traditionally considered high dietary sources of purines. In these and other scenarios, data

for the purine content of specific foods can be beneficial for making food choices and optimizing established healthy dietary patterns for adults at risk for gout.

C. The Need for Purine Data

Estimating Total Intake of Various Purines is Challenging

There have been few, if any, well-controlled trials documenting the relationship between the consumption of dietary purines and serum urate in healthy individuals or in those with hyperuricemia or diagnosed gout. One of the major hurdles in conducting such intervention studies and other types of clinical trials is that the exact amounts of individual purines in most foods, and especially in cooked foods, are unknown (Gibson et al., 1983; Choi et al., 2004). Additionally, the bioavailability of different purines varies considerably in specific foods, so total purine content alone is insufficient - it is also important to know what specific purines are present. For example, studies which supplemented subjects' diets with RNA or DNA showed that RNA influenced urate concentration more than an equivalent amount of DNA (Zollner & Griebsch, 1974). Other dietary studies have found that oral doses of adenine and hypoxanthine increased subjects' SU levels while guanine and xanthine had no effect (Clifford et al., 1976). Overall, very few intervention trials have been conducted in recent years to examine how individuals with hyperuricemia respond to dietary changes.

We are not aware of research conducted to establish dietary guidance on intakes of various purines. While recommended intake levels for purines have been established internationally, such as Japanese recommendations limiting purine intake to 400 mg/day to prevent hyperuricemia and gout (Kaneko et al., 2020), current U.S. dietary guidance does not provide recommended intake levels of various or total purines for healthy adults or patients with hyperuricemia. The American College of Rheumatology rated the certainty of evidence as "low" between limiting purine intake and gout management in its recent review (FitzGerald et al., 2020), but it has been noted that there was a dose-response relationship between higher consumption of purines and risk for gout flares (acute episodes of joint pain and swelling) (Zhang et al., 2012). These gaps suggest the need for more research to determine if diet-disease relationships do exist, as well as the need for research and clinical resources such as databases that will improve estimation of total and individual purine intake.

Data are Lacking for Purines in Foods and Dietary Supplements

There is very little high-quality information available on the purine content of commonly consumed U.S. foods. Systematic searches for sources of purine food composition data for dietary guidance to assist patients or clinicians reveal that data are rarely or poorly documented or are outdated. Websites focusing on gout treatment often provide only limited total purine values and do not give data on which purine bases are present in foods, nor do they cite their data sources. A table of purine values is provided in the seminal food composition reference (Pennington & Spungen, 2012), although it is not in the public domain, there is a fee for accessing these data, and the data are outdated and limited to that available over a decade ago.

Some dietary guidance sources group foods into categories (low, medium, high, very high) using a nominal scale or an ordinal scale (numbering 1 through 4) to guide patients on which foods are high in purine content and should be restricted in frequency and amounts consumed. Such categorizations should be based on consistent sampling and assay methodology and should be relevant to the food supply of the

patient's country of residence if they are to provide actionable and effective guidance. Many other patient-facing materials on health websites (e.g., Cleveland Clinic or WebMD) and patient advocacy groups (e.g., the Arthritis Foundation) provide similar recommendations for restricting purines, but they often focus on rarely or uncommonly consumed foods (e.g., game and organ meats) and neglect commonly consumed foods in the U.S.

Also, no North American-based studies have published analytical data on the purine content of commonly sold DS available for U.S. consumers. However, concentrated amounts of purines have been found in some Japanese DS (Kaneko et al., 2014), suggesting that DS potentially could represent a substantial source of purines intake. Some DS on the U.S. market, such as products promoted for increasing energy or losing weight, are labeled as containing purine nucleotides or related compounds (e.g., adenosine, ATP, GTP) or purine-rich constituents (e.g., yeast extracts). Many other DS may have purines as an undisclosed significant component but are not required by law to specifically list purines in the Supplements Facts panels. These products could pose a health risk to people who must limit their purine intake and are unaware that the products contain purines.

The absence of a centralized and consistently structured database is problematic for at-risk groups such as patients already suffering from hyperuricemia and gout because it has led to poorly documented guidance and the proliferation and use of anecdotal home remedies. Data for the purine content of foods and DS are limited and needed to strengthen the science base between purine intakes in health and disease outcome, as well as to address other gaps in knowledge of their physiological relevance (Choi et al., 2004).

D. Creation of the USDA Purine Database

Purpose

The "USDA and ODS-NIH Database for the Purine Content of Foods" is designed to function as an essential source of publicly available dietary purine data for researchers, health professionals, and others striving to monitor purine consumption (USDA & NIH ODS, 2021). The purine database was developed as a collaborative effort among scientists at USDA's Methods and Application of Food Composition Laboratory (MAFCL) in Beltsville, MD, the Office of Dietary Supplements National Institutes of Health (ODS-NIH) in Bethesda, MD, the University of Florida Clinical and Translational Science Institute Southeast Center for Integrated Metabolomics (UF CTSI-SECIM) in Gainesville, FL, the Beth Israel Deaconess Medical Center in Boston, MA, and the Department of Animal and Food Sciences at Texas Tech University in Lubbock, TX.

The first USDA and ODS-NIH purine database release (Release 1.0) was published on the USDA MAFCL website in February 2023. Release 1.0 of the database provided existing data for purine bases in foods (396 foods and 15 alcoholic beverages) sourced from mostly non-U.S. validated literature with a usable format.

Release 2.0 of the database contains new analytical data for 61 foods and 14 purine-containing DS from samples collected from the U.S. market, as well as all validated literature data that was published in Release 1.0 to allow for comparisons among foods. The goals of this study were as follows: a) to generate new analytical data for the purine database for commonly consumed U.S. foods using validated methodology based on nationally representative intake patterns, b) to ascertain the purine content of the top consumed meat products sold in the U.S., c) to observe possible changes in the content or base form

of purines and uric acid after cooking, and d) to determine the analytical content of purine-containing DS from a subset of commonly consumed supplement products. Foods and DS selected for analysis were based on comprehensive and representative sampling plans detailed below which were designed to address data gaps observed after the publication of Release 1.0.

Database Format and Reporting Protocols

The Purine Database Release 2.0 is presented as an Excel data file, which contains a total of 6 tabs. Tabs are separated into North American food data (United States and Canada), international food data, alcohol data, DS per serving unit (per individual unit such as one tablet, one capsule or a specific weight), DS per serving (e.g., a recommended intake such as two tablets or three capsules), and literature-derived purine content. Data were grouped into typical U.S. food categories for presentation in the database (e.g., beef organ meats, legumes, vegetables). USDA's analytical data are presented in bolded text along with the values from other literature that was reviewed to enable interpretation and for planning future work. Sample size (n), the four major purine bases (adenine, guanine, hypoxanthine, xanthine), and their total sum are all reported. Uric acid was added in this release due to measurable amounts found in some foods. Footnotes are given where further descriptions or explanations of specific foods are needed.

Means, standard error of the mean (SEM), minimum (Min), and maximum (Max) values were reported as milligrams per 100 grams for foods and in milligrams per 100 milliliters for alcohol. When applicable, other reporting units from literature were converted into these units for consistency in observing data across studies. Food data is recorded on a fresh weight basis and cooked basis for some foods. Data cells with a dash ("- ") indicate data that was not calculable or measured, whereas values listed as "ND" (not detected) in literature were reported when purine measurements were below the studies limit of detection.

Dietary supplements are presented as 5 categories (brewer's yeast, chlorella, spirulina, RNA/DNA (nucleotide complex), and royal jelly), and are grouped under their respective dosage forms (capsule, tablet, powder) to best represent the purine content associated with ingestion of each form. DS were reported as milligrams per serving unit and as milligrams per serving in accordance with their respective Supplements Facts panels.

<u>Literature Purine Data</u>

1. Data Sources

For Release 1.0 published February 2023, published data for four purine bases (adenine, guanine, hypoxanthine, and xanthine) in foods and alcoholic beverages were compiled. Food listings from literature were reported in fourteen studies conducted in various countries. Data came primarily from Japan; less than 20% of the food items in the database were from North American sources (United States and Canada).

Data from the scientific literature were re-examined in 2024 to obtain an accurate number of foods and to determine which studies, if any, measured uric acid in food; only one of the fourteen studies contained this information. Six foods from Kaneko et al. (2014) were separated into two different food descriptions based on an incorrect grouping of data. The food descriptions modified in Release 2.0 were:

- Beef brisket (split into beef brisket and beef shin)
- Red king crab (split into red king crab and snow crab)

- Bean sprouts (split into “with” and “without bean” descriptors)
- Mustard spinach (komatsuna) (split into “baby” and “mature” varieties)
- Spinach (split into “baby” and “mature” varieties)
- Removal of the food longcod (split into arabesque greenling and fat greenling)

Footnotes were also added to three foods from Kaneko et al. (2014) (white rice, asparagus, and bamboo shoots) to indicate when USDA combined data for the same food due to similar purine measurements and processing conditions.

Tab 1 displays 75 foods from North American sources to facilitate inspection of data for foods analyzed domestically. Tab 2 reports 327 foods from other countries to provide a broadened perspective of available published data. Tab 3 includes 13 alcoholic beverages from Japan, Austria, Hungary, Romania, and Poland. Food data from countries beyond North America can be applicable in the U.S. due to availability in Asian or other specialty markets. However, differences among plant species, growing conditions, storage, laboratory methods, and other factors can impact reported purine values and should be considered when referencing data from various sources.

The studies were published between 1976 and 2020, with nearly half of them occurring prior to 1989. Other studies were found but were not included because they reported total purine values but not values for individual bases or disseminated their data only in the German or Japanese languages.

2. Analytical Laboratory Methodology

Analytical laboratory methods for measuring purine content in the foods and beverages in the database are listed with their respective data sources in Tab 6. High performance liquid chromatography (HPLC), which has been proven to be effective for many years in measuring purine content of foods, was used in all the published studies except for one, which used capillary zone electrophoresis for analysis of beers.

3. Data Evaluation Methods

The purine literature data were evaluated for quality using procedures developed by scientists at USDA’s MAFCL, (formerly the Nutrient Data Laboratory) (Bhagwat et al., 2009). The scientists used a modified version of the USDA Data Quality Evaluation System (DQES) to assign a numeric score to each data source (Holden et al., 2002, 2005). Five categories of documentation were initially evaluated: sampling plan, sample handling, number of samples, analytical method, and analytical quality control. However, scoring of the analytical method could not be accomplished due to lack of standardized evaluation criteria. Notable characteristics of the studies reporting data used in this purine database (except for additional data published in 2020) were reported in Wu et al., 2019.

4. Literature Data Discussion

As observed in Tabs 1 and 2, purine content varied among foods, and it also varied for the same food in different studies. For example, total purine in raw beef cuts in the database ranged from 77 to 123 mg/100 g (chuck ribs and round, respectively), while liver had up to 220 mg/100 g. Among canned seafood items in the database, clams had 62 mg/100 g, while anchovies had 321 mg/100 g. Furthermore, the overall category of finfish and shellfish ranged from 7.7 to 1,400 mg total purines/100 g.

Dark and traditional-type beers had higher adenine and hypoxanthine values than other types of beers and other alcoholic beverages reported, although the highest total purine value among alcoholic beverages was only 13.5 mg/100 g (or about 46 mg/12 ounce serving) (Tab 3).

Uric acid was evaluated in vegetarian dishes, soy protein concentrate, and poultry (Tab 2). Negligible uric acid was observed in most of the vegetarian dishes and the soy protein concentrate. Raw chicken liver contained 51 mg uric acid/100 g; this value corroborates prior scientific consensus that purine metabolism occurs in the liver prior to excretion via the intestines and renal system.

Variations in purine content may be due to natural differences in foods (such as vegetable cultivars or animal breeds), different sampling plans, sample handling, cooking, laboratory methods, and other factors. Overall, purine values are generally highest in animal-based products (especially organ meats) and lowest in dairy, eggs, grains, fruits, and most vegetables. Moreover, in most cases products from animal sources (other than dairy and eggs) contain higher amounts of the uricogenic bases hypoxanthine and adenine than other food groups. The food category with the highest mean hypoxanthine values was the "soups and sauces" group which was mostly influenced by the dehydration process and reporting of certain sauces as mixes, not as consumed. Thus, the user of the data would need to account for the dilution factor of water to correct to "as consumed." Mean hypoxanthine levels were lowest in plant-based foods, dairy, eggs, and sweets. Mean values for adenine were highest in organ meat products (chicken and beef liver, pork kidney), dried yeast, and cod milt (i.e., the cod's sperm filled gland) and were lowest in dairy and eggs, fruits, and sweets.

USDA Analytical Purine Data

1. USDA Samples: Sources and Sampling

Food Samples

USDA food samples came from several sources and included both archived and recently acquired material. Recently procured samples were preferred whenever possible to provide data that best represented the current U.S. food supply. Therefore, most USDA samples for purine analysis were acquired in conjunction with the FoodData Central (FDC) Foundation Foods (FF) program, a new food composition database designed to provide expanded metadata on a diverse number of raw foods and ingredients (USDA ARS, 2024a). Foods from this program are primarily convenience-sampled with the goal of collecting a diverse and representative number of samples from manufacturers and distributors. Foods were obtained at large grocery stores throughout Maryland and Virginia from January 2023-2024. All samples were processed by the food composition laboratory at Virginia Tech in Blacksburg, VA.

A few of the foods selected to address data gaps were from the National Food and Nutrient Analysis Program (NFNAP) (Haytowitz and Pehrsson, 2018). Among these were cooked chickpeas, canned tuna, and 2% milk (collected in July 2010, January 2017, and April 2018, respectively).

To determine the purine content of animal-based products and the effects of cooking, 13 types of meat were selected based on 2017-2018 consumption data published in 2020 from the What We Eat in America (WWEIA) database, the dietary intake interview portion of the national food survey NHANES (USDA ARS, 2024b). Meat samples were purchased with unique lot numbers from different manufacturers in Lubbock, TX supermarkets in June through October 2023 through collaboration with Texas Tech

University (TTU). Meats were stored in a food-grade refrigerator (4 °C) after purchase. Meats were chopped into pieces, placed in a strainer, and were submerged into liquid nitrogen until solidly frozen. Samples were subsequently homogenized with a blender, placed in double-sealed plastic bags (Ziploc brand), and were frozen at -20 °C or colder until ready to aliquot. All samples were processed prior to expiration dates listed on the packages. The meat samples were cooked at TTU based on a raw-to-cooked paired meat sampling plan (Table 2). Subsamples of raw or unprepared (for processed foods) material were collected from each meat cut before cooking to allow for a direct comparison of purine content. Processed meats were prepared for analysis according to label directions (e.g., boiling). Raw meats were cooked without added ingredients such as oils, spices, and/or butter. Conventional recipes that most closely emulated American consumers' cooking methods for each meat were used.

Samples for purine analysis were shipped to the University of Florida Clinical and Translational Science Institute Southeast Center for Integrated Metabolomics (UF CTSI-SECIM) in Gainesville, FL. Typically at least 6 to 8 individual samples per food to were obtained to provide a representative sample size (n) for statistical analysis. However, for some foods, a smaller (n) was deemed adequate due to their low observed variability, material limitations, or the exclusion of outlier data. Blind duplicates and replicates were included for most foods.

In some cases, literature data was used to identify foods critical in U.S. diets warranting additional analysis due to low (n) or lower than expected purine content. For example, only one data point was observed in literature for chicken eggs, which reportedly did not contain purines (Kaneko et al., 2014). Therefore, a total of 6 raw chicken eggs were convenience sampled from supermarkets (n = 3) and a local farm (n = 3) in Alachua, FL, in September 2024. Each set of eggs were boiled in liquid chromatography (LC) grade water for approximately 8-10 minutes until fully cooked. Samples were subsequently peeled, and the egg whites and yolks were separated. The egg whites were chopped finely with a knife, while the yolks were crushed with a fork.

Dietary Supplement (DS) Samples

A sampling plan was developed by USDA to identify and procure DS with the overall goal of obtaining analytical purine content from a subset of commonly consumed supplements. The sampling plan was based on a thorough evaluation of published literature, U.S. market data from online web searches using the ODS Dietary Supplement Label Database (DSLD) and retail vendors, analytical data from Kaneko et al. (2014), and an intake analysis on a representative sample in the U.S. population using the US National Health and Nutrition Examination Survey (NHANES) data spanning 2017-2020. Five DS categories containing "very high" levels of purines (>300 mg/100 g) were chosen: brewer's yeast, chlorella, royal jelly, RNA/DNA (nucleotide complex), and spirulina. Searches of NHANES DS data files with these key terms led to the identification of 38 potentially high-purine products available in the U.S. market.

A USDA in-house, ranked scoring system was used to prioritize the most popular DS available for purchase by U.S. consumers (Table 1). A score of "2" was given to products found in NHANES due to their use by American consumers, and "1" to products found in DSLD and online retail websites including Amazon, Walmart, and others. A variety of online retail platforms were researched /surveyed to ensure that a diverse range of purine-rich DS were represented. Ultimately, 14 representative DS samples characterized by 3 dosage forms (tablet, capsule, and powder) were selected for inclusion in the Purine Database Release 2.0.

Supplements were procured by USDA and UF CTSI-SECIM from online retailers including Amazon, iHerb, and manufacturer websites. For each sample, at least 200 pills of the same lot with an expiration date of at least one year were purchased.

Table 1. List of dietary supplements (DS) identified for purine analysis using USDA's US market-based sampling plan.

Product Name (dose)	Dosage Form	Brand Code	NHANES	DSLD	Online Retail Vendor						USDA score
					Amazon	iHerb	Walmart	Pureformulas	Vitamin Shoppe	Other	
Brewer's Yeast, 650 mg	Tablet	A	0	1	1	1	1	1	0	0	5
Brewer's Yeast, 500 mg	Tablet	B	0	1	1	1	1	0	0	0	4
Brewer's Yeast, 500 mg	Tablet	C	0	1	1	1	1	0	0	0	4
Brewer's Yeast, 1000 mg	Capsule	J	0	0	1	0	1	0	0	1	3
Chlorella, 200 mg	Tablet	D	2	1	1	1	1	1	1	0	8
Chlorella, 1000 mg	Tablet	A	0	1	1	1	1	1	0	0	5
RNA/DNA (nucleotide complex)	Capsule	F	0	1	1	1	1	1	0	0	5
Royal Jelly, 1500 mg	Capsule	A	0	1	1	1	1	1	0	0	5
Ginseng & Royal Jelly	Capsule	A	0	1	0	1	1	1	0	0	4
Spirulina, Blend	Powder	E	2	1	0	0	0	0	0	1	4
Spirulina, 1000 mg	Tablet	G	2	1	1	1	1	1	1	1	9
Spirulina, 500 mg	Tablet	H	2	1	1	1	1	0	0	0	6
Spirulina, 500 mg	Tablet	I	0	1	1	1	1	0	0	0	4
Spirulina, 500 mg	Tablet	A	2	1	1	1	1	1	0	0	7

A score of "1" was given to products found in DSLD and online retail websites including Amazon, Walmart, and others, and a score of "2" was given to products found in NHANES due to their use by American consumers.

2. Analytical Laboratory Methodology and Quality Control

Sample Preparation and Extraction

All food samples except for chicken eggs (as described above) were homogenized prior to shipment at UF CTSI-SECIM. Upon arrival, samples were transferred into a freezer and stored in -80 °C until analysis. Unprocessed dietary supplements were stored at room temperature.

The United States Pharmacopoeia (USP) has developed analytical reference standards in the form of monographs and general chapters for dietary and herbal supplements. However, monographs for the 5 categories of purine-containing DS do not exist. Therefore, for the preparation of supplements, a total of 20 pills (30 if pills were ≤ 20 mm) per DS were homogenized following USP general guidance (U.S. Pharmacopoeia (USP), <2040>). Tablets and capsules (along with the shell) were homogenized using a coffee grinder. The jars were cleaned out between grinding with deionized water and methanol. The fine, powdered sample was processed as-is without further homogenization. Resulting material was prepared in duplicate, and remaining material was stored at -80 °C for retesting as needed. Additionally, brewer's yeast tablets from the same batch of material were prepared and analyzed individually a total of 6 times for reproducibility.

Purines were extracted using acid hydrolysis according to previously published methodology with minor modification (Kaneko et al., 2014). 1.0 g of material was transferred to a 16-mL glass tube. Ten mL of liquid chromatography–mass spectrometry (LC-MS) grade water was added to each sample along with 0.5 mL of 2,6-diaminopurine as an internal standard. Samples were sonicated using a high-powered sonicator (Model #FS-220, Fisher Scientific, Waltham, MA) for 15 minutes.

Acid hydrolysis was performed by adding 3 mL of 70% perchloric acid ($HClO_4$) solution with heating in a water bath for 60 minutes at 95 °C. The samples were then neutralized by adding 3.5 mL of ammonium hydroxide (NH_4OH) to pH 8.0. Samples were filtered through a Grade 1 Whatman qualitative filter paper (70 mm diameter) (Cytiva, Wilmington, DE). An aliquot of the filtrate was transferred to a clean tube along with 20 µL of purine internal standards and 200 µL of precipitation solution (45:5 acetonitrile:acetone with 0.01% ammonium hydroxide). Samples were centrifuged at 20,000 x g for 10 minutes at 4 °C before transferal to HPLC vials.

Qualitative and Quantitative Analysis

Purine content was determined using Hydrophilic Interaction Liquid Chromatography coupled with Tandem mass spectrometry (HILIC-HRMS/MS). Samples were analyzed using a Thermo Scientific Vanquish UHPLC system coupled to a Thermo-Scientific Q-Exactive orbitrap mass spectrometer operated in negative electrospray ionization mode. Chromatographic separation was performed using a HILIC-Z column (1.9 µm, 2.1 mm X 150 mm; Agilent, Santa Clara, CA). Mobile phase A was 15 mM ammonium formate (NH_4HCO_2) in 1:9 water: acetonitrile (pH 9.9) and mobile phase B was 15 mM ammonium formate in 9:1 water: acetonitrile (pH 9.9). The pH was adjusted with ammonium hydroxide. Both mobile phases were spiked with 0.5% medronic acid ($CH_6O_6P_2$). The injection volume was 3 µL with a flow rate 0.4 mL/min.

A mixture of purine standards (xanthine, hypoxanthine, guanosine, guanine, adenine, inosine, AMP, IMP, GMP and uric acid) was prepared at a concentration of 500 µM and a mixture of internal standards (inosine-$^{15}N_4$, adenine-$^{15}N_5$, xanthine-^{13}C,$^{15}N_2$, hypoxanthine-^{13}C,$^{15}N_2$, guanosine-$^{13}C_2$,^{15}N, and AMP-

$^{13}C_5$; ≥ 95% purity) was prepared at a concentration of 10 µg/mL. This mixture of internal standard was spiked into each calibration level and samples. A ratio of area under the curve for each analyte to the area under the curve for the respective internal standard was plotted to calculate the amount of each analyte in the sample. Using this stock mixture of standards, an external calibration curve ranging from 50 ng/mL to 25,000 ng/mL was prepared. For hypoxanthine, a separate external curve was prepared with concentration range 250 ng/mL to 400 µg/mL.

Quality Control

Quality control (QC) samples were prepared from separate stock solutions of purine standards at three levels: 750 ng/mL, 2500 ng/mL and 7500 ng/mL. Hypoxanthine QC levels were prepared at 750 ng/mL, 7500 ng/mL, 25000 ng/mL and 75000 ng/mL. QCs were acquired every 10 samples to check the performance of the instrument and stability of the analytes throughout the batch. Blind duplicates and/or replicate material were included in each batch of analyses to evaluate the repeatability and reproducibility of the data. The limit of detection (LOD) for purines in food and DS samples was 50 ng/mL. Sample error for all the analyses was maintained under 15% to account for the inherent variability of foodstuffs.

3. Data Discussion

Food Samples

USDA's analytical laboratory data (Tab 1) shows the purine content of food varies depending on category, food type, cultivar, cooking status, and more. Foods in the meats and seafood categories contained more purines than foods in the dairy, legumes, and vegetables categories. Variation in purine content was also observed within food categories. For example, the total amount of purines in pork products ranged from 141 to 448 mg/100 g depending on the meat cut, processing state, and cooking status. Similarly, the total quantity of purines in raw and processed seafood ranged from 110 to 260 mg/100 g depending on the fish and crustacean species. Notably, the purine content measured in most of USDA's meat samples were higher compared to literature values apart from the turkey values. In some cases, foods which were higher or lower in purine content than expected compared to the rest of the foods in a category were observed. These included green peas, which were higher in total purines (72 mg/100 g), and cooked chickpeas, which were lower in total purines (11 mg/100 g) compared to other legumes which ranged from 21 to 35 mg/100 g. Less than 1.0 mg/100 g total purines were measured in chicken egg whites and yolks, which is comparable to data in Kaneko et al. (2014). This analytical data is consistent with dietary guidance classifying meat and seafood as purine-rich foods.

Care should be taken in interpreting differences between the raw and cooked meats. For all raw to cooked paired meat products, total purine content on a milligram per 100-gram basis increased due to moisture and fat losses from cooking (Table 2). For example, raw bacon appeared to contain over three times more total purines than cooked bacon (141 vs. 448 mg/100 g). When moisture loss from cooking was considered, negligible differences between the purine content of the two products were observed. Processed meats (e.g., frankfurters), however, retained their total purine content before and after boiling because they were already pre-cooked and ready-to-eat (RTE). These findings suggest that cooked meats should be considered when developing sampling plans for the analysis of purine content in foods. Furthermore, the inclusion of these products in databases could facilitate more accurate dietary estimations of total purine intake.

Table 2. Meat cooking methodology at Texas Tech University and moisture losses after cooking.

Meat	Cooking method[1]	Cooking condition	Weight loss (%) (Mean ± SD)
Frankfurter (beef)	Boiled	Boiled in deionized water for 4-5 minutes	7.52 ± 1.35
Frankfurter (mixed meat)	Boiled	Boiled in deionized water for 4-5 minutes	4.36 ± 1.95
Ground Beef (73% lean)	Pan-fried	Cooked in skillet at 400°F (204.4°C) until internal temperature reached 165°F (73.8°C)	49.59 ± 0.93
Ground Beef (93% lean)	Pan-fried	Cooked in skillet at 400°F (204.4°C) until internal temperature reached 165°F (73.8°C)	35.08 ± 4.90
Bacon	Pan-fried	Cooked in griddle at 400°F (204.4°C), flipped every 3-4 minutes until internal temperature reached 145°F (62.8°C)	70.06 ± 2.42
Pork Sausage	Pan-fried	Cooked in skillet at 375°F (190.6°C) for 2 minutes and 15 seconds on each side until internal temperature reached 155°F (68.3°C)	29.34 ± 5.76
Chicken Breast	Roasted	Cooked in oven to 375°F (190.6°C) until internal temperature reached 165°F (73.8°C)	25.29 ± 3.22
Pork Loin	Pan-fried	Cooked in griddle at 400°F (204.4°C), flipped every 5-6 minutes until internal temperature reached 165°F (73.8°C)	36.80 ± 4.24
Beef Chunk Roast	Braised	Braised in Dutch oven at 250°F (121.1°C) with deionized water until internal temperature reached 185°F (85.0°C)	35.04 ± 4.50

[1] Meats were prepared without added oils, spices, butter, or other added ingredients

There was stratification of uricogenic bases across categories and food types. Hypoxanthine was the predominant purine base found in meats and seafood, whereas dairy, vegetables, and legumes were primarily composed of adenine and guanine. The foods' purine composition remained stable after cooking except for ground beef ("73% lean meat / 27% fat" and "93% lean meat / 7% fat"). In these samples, an increase in the percentage of hypoxanthine and decreases in the percentages of adenine, guanine, and xanthine after cooking were observed. These results suggest not all purines are distributed equally in and across food types, and that for some foods, their purine composition may be impacted by heat and processing factors. More research is warranted, but it is clear from these data that purine base composition should likely be considered alongside total purine content when implementing dietary modifications.

Concentrations of uric acid in foods were measured and reported when they were present in the database as a foundation for future research. Uric acid was not detected in most samples because it does not exist in plants, and it is not the final metabolic product for almost all animal foods and seafoods studied. The presence of uric acid in animal foods has only been reported in one publication (Havlik et al., 2010), in which a significant amount of uric acid (51 mg/100 g) was detected in chicken liver. Chicken legs and beef were also found to contain low levels of uric acid.

There are also studies on certain crustaceans, including American lobster (Battison, 2013) and land crab (Horne, 1968), that report that these species have high blood and/or urine uric acid levels. In USDA data, crab contained 32 mg/100 g uric acid. In addition, concentrations less than 1.0 mg/100 g were observed in

other foods including beef, dairy, poultry, sausage, and seafood categories. Unlike purines, the bioavailability of dietary uric acid is largely unknown, although it is known that it can be potentially absorbed through uric acid transporters in the intestine. The impact of uric acids in foods on SU levels has not been studied, but the topic certainly warrants further research.

When differences in USDA's data exist compared to published values from the literature, they may be attributable to vegetable cultivars, animal species, geographic differences, agricultural and animal husbandry methodology changes over time, and manufacturer processing disparities. The studies' sampling plan methodologies and analytical instrumentation may have also impacted measurements. Statistical comparisons between USDA and literature data were not possible due to low (n) and data access limitations. Overall, the finding in this study highlight a need for current data on the purine content of foods, and a reevaluation of dietary guidance based on this for populations interested in lowering purine consumption.

Dietary Supplement Samples

To facilitate analysis, products from the 5 DS categories were grouped based on their dosage form (tablet, capsule, and powder). For instance, all brewer's yeast tablet product results were averaged and included in the database as one entry. This approach consolidated 14 total products into 7 entries in the database, with each representing a distinct dosage form.

Dietary supplement data is presented in two formats: as "per serving unit" (Tab 4) and as "per serving size" (Tab 5). The analytical results indicate that purine content in DS varied significantly across categories, dosage form, and brand. Chlorella tablets exhibited the highest total amount of purines (76 mg/serving), while royal jelly capsules contained the lowest (1.5 mg/serving). In descending order of total purine content per serving, the ranking was as follows: chlorella [tablet] > nucleotide complex [capsule] > spirulina [tablet] > brewer's yeast [tablet] >spirulina [powder] > brewer's yeast [capsule] > royal jelly [capsule].

Adenine and guanine constituted over 90% of the total purines in all tested supplements. Notably, uric acid was not detected in any of the DS samples. An internal comparison revealed that USDA's analytical DS data (in mg/100 g) were consistently lower in average total purines compared to published literature values from Kaneko et al. (2014) apart from the spirulina tablet. This discrepancy is likely attributable to geographical differences and variations in manufacturing processes.

While the brewer's yeast capsule has a lower purine content per serving compared to brewer's yeast tablets, it is important to consider the recommended dosage of each product. One brewer's yeast tablet product suggests consuming 3 servings per day, with each serving consisting of 3 pills (totaling 9 pills daily). Therefore, on a per-day basis, the brewer's yeast DS analyzed in this study can provide a higher purine intake than other supplements, despite its lower per-serving value.

Finally, reproducibility was assessed to ensure analytical consistency among the DS. The relative standard deviation percentage for the total number of purines in brewer's yeast was 0.7, indicating good reproducibility of the sample preparation and extraction protocols.

E. Database Strengths and Limitations

This database has several strengths. To the authors' knowledge, this is the first study to examine the purine content in a commonly consumed purine-containing DS in the United States. Furthermore, the database provides information for the contents of purine bases in foods covering many different food categories, which were obtained from an extensive literature search and directly assayed analytical data. Literature data were based on research findings from studies whose published reports met the minimal criteria for inclusion using established data evaluation protocols. Compared to Release 1.0, USDA's new analytical data provides new and updated values for many foods collected from the U.S. market. The foods selected for analysis were expected to contain substantial amounts of purines or were analyzed to fill knowledge gaps. The selected foods are of relevance and importance to the U.S. population based on dietary intake patterns extrapolated from WWEIA.

In addition, the purine contents in raw and cooked pairs of selected commonly consumed meat products were included in the database. This data will assist with more accurate estimations of purine intake as most animal products are cooked before consuming. Another strength is that multiple samples were purchased and analyzed to understand variability. Finally, this analytical purine data allows for more accurate intake estimates. Thus, the database can be used by clinicians, public health researchers, and consumers to manage the dietary intake of purines and to facilitate treatment of subgroups diagnosed with hyperuricemia and gout.

Limitations of the database include the possible significant discrepancies between the literature data and USDA's analytical data. It should be noted that nearly half of all literature data in the database originated from studies performed 3 decades ago. Most of the literature data only presented a sample (n) of 1. Because of this and the small sample (n) observed in the studies, statistical comparisons between USDA's analytical data and literature data were not possible. The USDA foods selected for analysis were partially chosen based on their anticipated purine content presumed from literature data. Therefore, analytical data for some food categories (e.g., fruits and sweets) are not included in this release. The analytical values provide representative estimates of purine content in select foods, but do not necessarily represent values for the entire U.S. market due to the nature of convenience sampling and product formulation differences over time. Similarly, the DS published in this release are limited in sample size due to the scope of the pilot study and the dosage forms selected; additional analyses are necessary to improve representativeness.

F. Summary: Plans for Foods and Dietary Supplements in Future Data Releases

USDA's Purine Database Release 2.0 includes analytical values for 61 food listings from 8 food groups and 14 dietary supplements from a total of 5 categories. This release also includes previously published literature data from 14 published international studies for 401 food listings from 20 food groups and 15 alcoholic beverages. These literature data are useful in further strengthening the scientific evidence base for identifying additional U.S. foods for purine analysis and in determining foods of substantial purine content for which expanded sample sizes would be advantageous. These new, validated analytical purine data provide valuable insights into the purine content of commonly available foods and purine-rich DS in the U.S. and may be used for improving estimates of dietary purine intake. This database is dynamic and will be expanded in 2025 when additional analyses of U.S. foods become available.

USDA's MAFCL will continue to procure and analyze foods from the U.S. food supply relevant for estimating purine intake for the next data release. The long-term stability of purines may be assessed in foods frozen in storage. In addition, literature-derived purine data on foodstuffs and DS published after February 2023 will be identified and evaluated for potential inclusion using established criteria, and acceptable data will be added to the database.

Additionally, a list of products which represent the total market share of purine-containing DS available to U.S. consumers will be generated. New DS from each of the 5 categories will be selected for analytical testing using website-scraping data from Amazon and Walmart. The web scraping will harvest the top purine-containing DS for each category sold over a period of three months based on the: (1) total number of units sold (sales volume), (2) number of consumer ratings over the products' lifetime, (3) search result ranking, (4) Amazon "best seller" status, and (5) Amazon sponsorship status (i.e., the presence of paid advertisements when browsing products). DS identified from the web scraping will be evaluated under USDA's comprehensive DS sampling plan as detailed above.

A lot-to-lot variability study of the 14 purine-containing DS in this release is also planned to determine if there are observable differences in purine content due to supplement product reformulation and logistical and storage differences. Further testing may include organ meat-based and combination products (e.g., chlorella and spirulina combination products). The ability of dosage units to release purines will be assessed by dissolution and disintegration performance tests, including measurement of bioaccessibility through assay of purine bases during and after in-vitro digestion of these DS in INFOGEST (Brodkorb et al., 2019).

Information on the food and DS contents of various methylxanthines may prove a useful adjunct to this purine dataset due to their chemical similarity, as well. Methylxanthines are chemical derivatives of the purine base xanthine which are naturally present in some plants (e.g., cocoa and coffee beans, tea leaves, cola nuts, guarana, and yerba mate). Methylxanthines such as caffeine, theobromine, and theophylline act as central nervous system stimulants causing diuresis, cardiovascular and metabolic effects, bronchial relaxation, and gastric acid secretion (Franco, Oñatibia-Astibia, & Martínez-Pinilla, 2013). Caffeine decreases the concentration of urate by inhibiting xanthine oxidase activity (Chittoor & Voruganti, 2020). Relatedly, coffee consumption has shown an inverse association with gout incidence (Choi et al., 2007). Coffee consumption also has an inverse association with hyperuricemia in men but is associated with increased hyperuricemia in women (Li et al., 2018). On the other hand, tea consumption does not appear to be associated with hyperuricemia, urate levels, or gout (Zhang et al., 2017). Relevant foods and supplements could be assayed and included as data fields to allow better estimates of total dietary intake and as effect modifiers in studies of purine metabolism. A methylxanthine database containing analytical data from the USDA-NIH NFNAP program is planned for release.

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