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Study Review

Availability and quality of published data on the purine content of foods, alcoholic beverages, and dietary supplements*

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ABSTRACT

Gout, the most common type of inflammatory arthritis and associated with elevated uric acid levels, is a global burden. "Western" dietary habits and lifestyle, and the resulting obesity epidemic, are often blamed for the increased prevalence of gout. Purine intake has shown the biggest dietary impact on uric acid. To manage this situation, data on the purine content of foods are needed. To assess availability and quality of purine data and identify research gaps, we obtained data for four purine bases (adenine, guanine, hypoxanthine, and xanthine) in foods, alcoholic beverages, and dietary supplements. Data were predominantly from Japan, and very little from the United States. Data quality was examined using a modified version of the USDA Data Quality Evaluation System. Purine values in 298 foods/19 food groups, 15 alcoholic beverages, and 13 dietary supplements were reported. Mean hypoxanthine (mg/100 g) in the soups/sauces group was 112 and mean adenine in poultry organs was 62.4, which were the highest among all groups. Regular beer had the highest adenine (1.63 mg/100 mL) and hypoxanthine (0.96 mg/100 mL) among alcoholic beverages reported. Overall, purine was highest in animal-based products and beer. Data were limited in scope, food descriptions, and quality. Additional studies on purine content in U.S. foods may support gout management.

1. Introduction

Gout has been estimated to affect nearly 4% of American adults, based on the National Health and Nutrition Examination Survey (NHANES) 2007–2008 (Zhu et al., 2011). The incidence of gout increased more than two-fold between the 1960s and 1990s in the US (Zhu et al., 2011). This number has been continuously growing in recent years, likely due to significant changes in dietary habits, lifestyle, and increased prevalence of obesity (Zgaga et al., 2012).

Gout is associated with elevated uric acids, also known as hyperuricemia, which exceeds normal levels due to overproduction of uric acid, inefficient excretion of uric acid by the kidney, or both (Maiuolo et al., 2016). The American College of Rheumatology (ACR) recommended managing hyperuricemia through several domains, including pharmacologic management and diet/lifestyle modification (Khanna et al., 2012). Urate-lowering drugs, such as allopurinol prescribed by primary care physicians and rheumatologists, are standard pharmacologic treatments for hyperuricemia, but patients do not respond equally (Hayman and Marcason, 2009; Khanna et al., 2012). Diet and lifestyle modifications are widely viewed as advantageous for lowering serum urate, but are not sufficient alone to achieve effective serum urate levels in a large fraction of individuals with gout (Khanna et al., 2012). Therefore, a combination of medicine, diet, and lifestyle interventions may be the best approach for controlling elevated serum uric acid levels.

Dietary modification has long been practiced as a supplemental way to manage hyperuricemia (Pillinger and Keenan, 2008). A number of varied dietary factors, including severe calorie restriction, or high fat or protein intake, or consumption of high-purine foods, are known to elevate serum uric acid levels; however, purine intake has shown the

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biggest dietary impact on serum uric acid levels (Brulé et al., 1988). Physicians from ancient Greece and Rome were aware of the relationship of alcoholic beverages and the incidence of gout (Pillinger and Keenan, 2008). Moreover, between the 15th and 19th centuries, a group of European physicians noticed the link between alcoholic beverages and gout (Pillinger and Keenan, 2008). Epidemiologic studies, such as prospective cohort studies and cross-sectional studies, have confirmed that certain dietary patterns may influence the risk of developing hyperuricemia and gout (Choi et al., 2004a, b, 2005; Villegas et al., 2012; Zgaga et al., 2012). Increased risk of gout was associated with high levels of meat and seafood consumption; decreased risk of gout was associated with increased dairy intake, and no association was seen between moderate consumption of purine-rich vegetables or total protein and risk of gout (Choi et al., 2004a, 2005). In addition, a strong association between alcohol intake and the risk of gout was observed, although the degree of risk varied substantially based on the type of alcoholic beverage (Choi et al., 2004b). Beer consumption showed the strongest correlation among all types of alcoholic beverages to a larger risk of gout, while moderate consumption of wine did not confer risk (Choi et al., 2004b). Studies have also found an association between the consumption of sugar-sweetened beverages (SSB) and an increased incidence of gout or plasma urate (Choi and Curhan, 2008; Zgaga et al., 2012). Fructose has often been blamed as the causal agent (Choi and Curhan, 2008); however, it is still unclear which compound(s) present in SSB trigger the elevated serum uric acid concentrations or whether SSB are just an "unhealthy" marker in general (Zgaga et al., 2012). The relationship of coffee and tea consumption to the risk of gout has also been examined. Studies have found that long-term consumption of coffee is associated with lower risk of incident gout, but no association between gout and tea consumption (Choi and Curhan, 2007, 2010; Choi et al., 2007).

In humans, purine molecules are absorbed by the small intestine through metabolic processes and are ultimately degraded and excreted as uric acid in urine (Jinnah et al., 2013). Although different purines are related chemically, they are metabolized differently as indicated in Fig. 1 (Sarwar and Brulé, 1991; Jinnah et al., 2013). The molecular structures of the four purine bases are shown in Fig. 2. Adenine and hypoxanthine have been considered uricogenic bases that modify serum and urinary uric acid concentrations greatly, whereas guanine and xanthine have a minimal effect (Clifford and Story, 1976; Brulé et al., 1988; Sarwar and Brulé, 1991).

For hyperuricemia treatment in Japan, daily purine intake is restricted to 400 mg (Kaneko et al., 2014). In the U.S., general dietary recommendations from the American College of Rheumatology are grouped into 3 simple qualitative food categories to treat and prevent

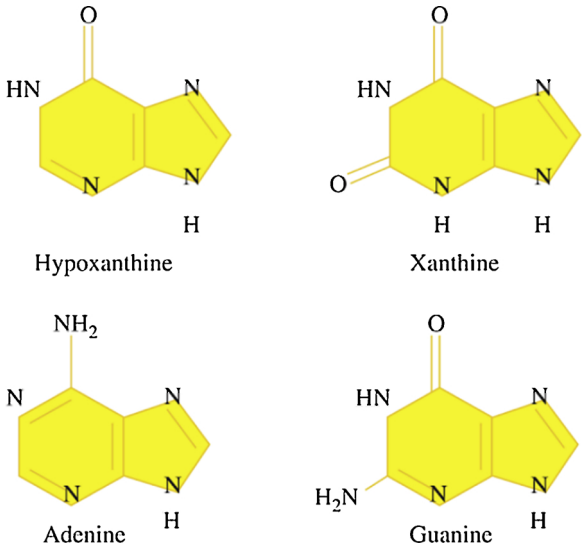

Fig. 2. Molecular Structures of Four Purine Bases (Kumari, 2017).

recurrent hyperuricemia, which are termed as "avoid", "limit", or "encourage" (Khanna et al., 2012). Patients with gout are advised to avoid organ meats high in purine (e.g., liver, kidney), high fructose corn syrup-containing products, alcohol overuse (more than 2 servings per day for men and 1 serving per day for women), and any alcohol use during gout flare-up periods; to limit their portions of beef, lamb, and pork, seafood with high purine (e.g., sardines, shellfish), naturally sweet fruit juices, table sugar, sugar-sweetened beverages and desserts, alcohol (particularly beer), table salt, and high sodium products (e.g., sauces, gravies); and are encouraged to consume vegetables and reduced-fat dairy products (Khanna et al., 2012). In addition, the Nutrition Care Manual by the Academy of Nutrition and Dietetics recommends the following: 1) drink 8 to 16 cups of fluids per day (at least half as water); 2) consume a moderate amount of protein; 3) follow a well-balanced eating pattern (i.e., Dietary Guidelines for Americans); and 4) intersperse purine-free days between days with meals containing purines if purine restriction is desired (Hayman and Marcason, 2009). Dietary recommendations in general reflect a lack of specific evidence from prospective, blinded, randomized clinical intervention trials in quantifying the safe limits for preventing and treating hyperuricemia and gout (Khanna et al., 2012).

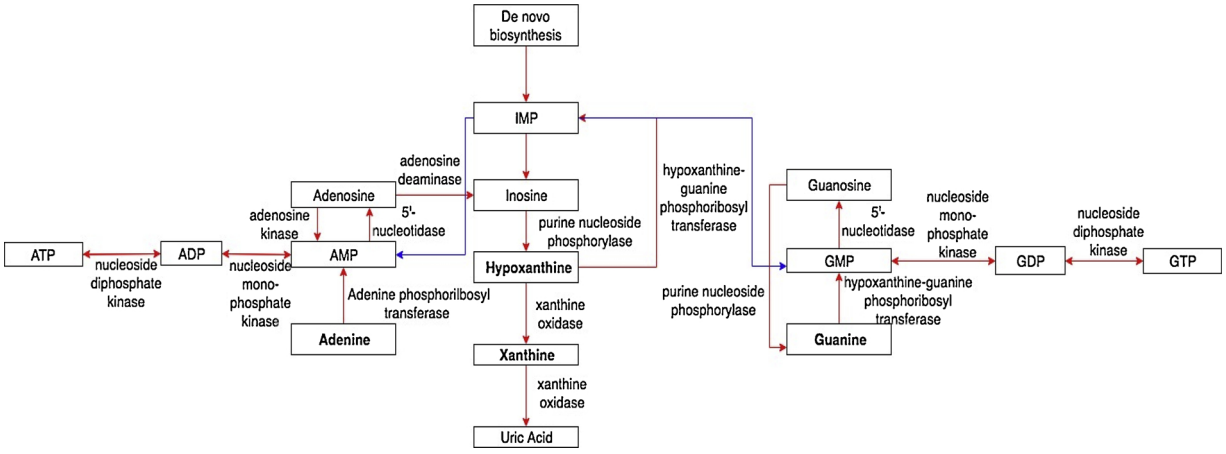

Fig. 1. Purine Metabolism (Jinnah et al., 2013).
Abbreviations: ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; GDP, guanosine diphosphate; GMP, guanosine monophosphate; GTP, guanosine triphosphate; IMP, inosine monophosphate.

2. Materials and methods

2.1. Literature search

An extensive literature review was conducted to obtain published assay results for purine bases in food, alcoholic beverages, and dietary supplements using databases of Google Scholar, PubMed, and Scopus. Only studies reported in English for the four main purine bases were included in this study. Foods processed or cooked *via* methods not commonly used in the United States (such as swordfish processed using a traditional Japanese method of soaking in sake lees) were excluded from the project.

2.2. Data compiling and cleaning

Published data were compiled using Microsoft Excel and Access. If a value was reported as "trace", that value was not included in analysis because no limit of quantification (LOQ) was provided in those studies. If a value was reported as "ND" (not detected), that value was viewed as zero across all studies. Unit conversion was performed to ensure cross-comparison among different studies. The standard unit used for purine content in foods was mg per 100 g wet weight and the standard unit in alcoholic beverages was mg per 100 mL. Purine contents that were reported on the basis of dry weight were converted to fresh weight using percentage of dry weight and the moisture value reported in the article. In cases where purine values based on dry weights were given without information on percentage of dry weight or percentage of moisture, purine values for those foods were excluded. The number of samples analyzed for each food item was noted, to report as the number of data points in the tables. Repeat analyses from the same homogenized sample, such as duplicates and triplicates, were considered as one data point.

2.3. Secondary data analysis

Mean, standard error of the mean (SEM), minimum (Min) and maximum (Max) values were calculated using the values reported in the identified publications. The mean values in this project were weighted to account for the different numbers of samples among the various sources studied. The weighted mean values were then used to determine the SEM based on the total number of samples across the various studies used. Values were rounded to 3-significant digits when more than 3-significant digits were reported or calculated.

2.4. Data quality evaluation

USDA Data Quality Evaluation System (DQES) is one of the first validated systems to assess analytical data quality across the international food composition network (Holden et al., 2002; Bhagwat et al., 2009). The five categories of factors of the DQES system are sampling plan, sample handling, number of samples, analytical method, and analytical quality control. The quality of each published resource in this study was initially scored for 4 out of 5 factors but the scoring process could not be completed, due to lack of standardized criteria for evaluating the analytical method of measuring purine. The dominant laboratory methodologies reported in the studies were reversed-phase high-performance liquid chromatography (HPLC) and cation exchange HPLC (Table 1). Capillary electrophoresis was used for purine quantification in one study (Table 1). The description of methodology was not clearly stated in all studies. Some studies failed to report their standards, limit of detection, and limit of quantification. In addition, the type and concentration of solutions used in hydrolysis varied across studies. Therefore, the degree of hydrolysis could also vary across studies, which would lead to considerable variations in comparison of values.

3. Results and discussion

Thirteen studies were included, predominantly from countries other than the United States, published between 1976 and 2017, with about half of the studies conducted before 1990 (Table 1). Studies were limited in scope, types and descriptions of foods, and data quality, especially for US foods. Considerable variation was observed in the purine content among the same foods evaluated in different studies.

3.1. Purine contents in food groups

The reported data were grouped according to typical U.S. food categories, in order to help guide interpretation for future work. The purine data reported in the source articles spanned 18 of the food groups in the USDA National Nutrient Database for Standard Reference (SR) (USDA, 2018); an additional food group was created to present data on vegetarian meat, fish and egg alternatives (Table 2). The mean hypoxanthine content (mg/100 g) was highest in the soups and sauces group (112 mg), with the high value influenced by dehydrated products in this group. Notably, powdered umami broth was nearly four-fold higher than any other soups, having 657 mg/100 g hypoxanthine, due largely to its inosine 5′-monophosphate (IMP) content (Kaneko et al., 2014). Mean hypoxanthine was high in the poultry products group (80.6 mg), compared to other groups. Mean hypoxanthine was lowest in plant-based foods, dairy and eggs, and sweets (0–7.79 mg). Mean adenine content (mg/100 g) was highest in organ products (46.1–62.4 mg), while it was lowest in dairy and egg products (2.04 mg), in fruits (0.85 mg), and in sweets (0.7 mg). In general, animal-based products (aside from dairy and egg products) contained larger amounts of the uricogenic bases (adenine and hypoxanthine) than were found in plant-based products (Fig. 3). This finding is consistent with the positive association between meat and seafood consumption and risk of gout or hyperuricemia found in epidemiological studies (Choi et al., 2004a, 2005; Villegas et al., 2012). Dairy and egg products, on the other hand, tend to contain a minimal amount of all four purine bases. This finding supports the reverse association between dairy intake and the incidence of gout or hyperuricemia (Choi et al., 2004a, 2005; Villegas et al., 2012).

3.2. Purine contents in individual food items

Dietary purine contents were compiled for 298 food items (details are provided in the Supplementary Material, Table S1), with food items arranged by groups and subgroups for ease of use. The food descriptions are those provided in the source documents, which in many cases were general rather than specific, such as "luncheon meat" with no further details. In cases where details were lacking, the term "unspecified" was added to descriptions on the table to differentiate them from similar listings. Individual purine values (minimum, maximum, mean value, and standard error of the mean, where available) along with the sources of data are provided.

Purine contents are also subject to change with food processing, cooking, and storage (Young, 1982, 1983; Lou, 1998; Lou et al., 2005). During storage, temperature and time are the main factors affecting purine content (Lou, 1998). Lowered storage temperatures reduce enzyme activity, which consequently slows nucleotide breakdown pathways and affects the patterns of purine base content (Lou, 1998). For example, storage of shrimp decreased total purine content of shrimp, at three different temperatures, over time (Lou, 1998). During processing of tilapia, the washing step reduced total purine content by about 60%, especially hypoxanthine and adenine, presumably because of their solubility (Lou et al., 2005). During cooking of chicken, moist heat methods and dry heat methods had similar effects on purine content, by increasing adenine and guanine slightly and by decreasing hypoxanthine in cooked products compared to their raw counterparts (Young, 1982, 1983). Using purine data requires excess caution when

Table 1
Summary of literature used in the data analysis.

Reference code	Sources of data	Year of publication	Country of origin	Analytical procedure	Number of food items	Number of samples per food item	Reported unit	Comments[a]
a	Brulé et al. (1988). Purine content of selected Canadian food products. *Journal of Food Composition and Analysis, 1(2),*130-8.	1988	Canada	Reversed-phase HPLC	31	1	mg/100 g	Provided method details including results for standards
b	Kaneko et al. (2014). Total purine and purine base content of common foodstuffs for facilitating nutritional therapy for gout and hyperuricemia. *Biological and Pharmaceutical Bulletin, 37(5)*, 709-21.	2014	Japan	Enzyme treatment; HPLC	270	1	mg/100 g	Reported analytical methods
c	Qu et al. (2017). Determination of four different purines and their content change in seafood by high-performance liquid chromatography. *Journal of the Science of Food and Agriculture, 97(2)*, 520-5.	2017	China	HPLC	19	3	mg/100 g	Provided method details including results for standards; reported CV* and % recovery; $n = 3$ analytical samples per food item
d	Kaneko et al. (2008). Purine contents of soybean-derived foods and selected Japanese vegetables and mushrooms. *Nucleosides, Nucleotides, and Nucleic Acids, 27(6-7)*, 628-30.	2008	Japan	Enzyme treatment; HPLC	31	1	mg/100 g	Provided brief methods information
e	Clifford and Story (1976). Levels of purines in foods and their metabolic effects in rats. *The Journal of Nutrition, 106(3)*, 435-42.	1976	USA	HPLC cation exchange	35	1	mg/100 g	Used internal standards
f	Havlik et al. (2010). Dietary purines in vegetarian meat analogues. *Journal of the Science of Food and Agriculture, 90(14)*, 2352-7.	2010	Czech Republic, Vietnam, Great Britain	Reversed-phase HPLC	42	1	mg/100 g dry weight	Provided method details including results for standards; reported CV* and % recovery
g	Sarwar et al. (1985). Purine content and protein quality of mechanically separated poultry meat products produced in Canada. *Canadian Institute of Food Science and Technology Journal, 18(3)*, 251-5.	1985	Canada	Reversed-phase HPLC	8	1	mg/100 g	Provided brief methods information
h	Young (1983). Effect of stewing on purine content of broiler tissues. *Journal of Food Science, 48(1)*, 315-6.	1983	USA	HPLC cation exchange	6	24	mg/100 g	Used standards; $n = 24$ analytical samples per food item
i	Young (1980). Evaluation of four purine compounds in poultry products. *Journal of Food Science, 45(4)*, 1064-5.	1980	USA	HPLC cation exchange	8	10/12/25	mg/100 g	Analyzed in duplicate w/in house materials; $n = 10$ to 25 analytical samples per food item
j	Young (1982). Purine content of raw and roasted chicken broiler meat. *Journal of Food Science*, *47(4)*, 1374-5.	1982	USA	HPLC cation exchange	4	12/16	mg/100 g	Analyzed in duplicate w/in house materials; $n = 12$ to 16 analytical samples per food item
k	Fukuuchi et al. (2013). A simple HPLC method for determining the purine content of beer and beer-like alcoholic beverages. *Analytical Sciences*, *29(5)*, 511-7.	2013	Japan	Enzyme treatment; HPLC	13	1	mg/100 mL	Reported analytical validation method, results of standards, % CV and % recovery
l	Kaneko et al. (2009). Determination of purine contents of alcoholic beverages using high performance liquid chromatography. *Biomedical Chromatography*, *23(8)*, 858-64.	2009	Japan	HPLC	55	1	μmol/L	Developed HPLC method for alcohol; reported results of standards, %CV, and % recovery
m	Klampfl et al. (2002). Determination of purines and pyrimidines in beer samples by capillary zone electrophoresis. *Analytica Chimica Acta*, *454(2)*, 185-91.	2002	Austria, Hungary, Romania, Poland	Capillary zone electrophoresis	16	1	mg/100 mL	Provided method details including results for standards

[a] CV = coefficient of variation; QC = quality control.

Table 2
Purine content of food groups (mg/100 g wet weight, edible portion).

Food Group	Nutrient Name	N	Mean	Standard Error of the Mean	Minimum	Maximum
Beef organ products	Adenine	11	46.1	7.98	12	95.8
	Guanine	11	44.7	9.08	12	97.3
	Hypoxanthine	11	35.2	5.52	0	96.6
	Xanthine	11	39.1	9.22	0	112
Beef (other than organs)	Adenine	15	16.7	1.09	7.2	27.1
	Guanine	15	11.8	0.60	7.6	15.9
	Hypoxanthine	15	62.2	3.94	36.7	87.2
	Xanthine	15	11.8	0.89	3.42	22.5
Cereal grains and pasta	Adenine	17	11.9	2.57	0.0	36.1
	Guanine	17	15.8	3.52	1.0	57.2
	Hypoxanthine	17	2.48	1.89	0.0	31.9
	Xanthine	17	1.40	0.55	0.0	7.3
Dairy and eggs	Adenine	8	2.0	1.02	0.0	8.2
	Guanine	8	1.99	0.62	0.0	4.2
	Hypoxanthine	8	0.19	0.12	0.0	1.5
	Xanthine	8	0.19	0.08	0.0	0.6
Finfish and shellfish	Adenine	161	32.0	2.72	0	258
	Guanine	161	85.7	16.77	0.0	1219
	Hypoxanthine	161	68.7	5.17	0.0	512
	Xanthine	161	18.0	3.12	0.0	268
Fruits and fruit juices	Adenine	3	4.1	3.26	0.5	10.6
	Guanine	3	3.47	2.02	1.2	7.5
	Hypoxanthine	3	0.3	0.12	0.1	0.5
	Xanthine	3	0.0	0.0	0.0	0.0
Lamb, veal, and game organ products	Adenine	2	31	–	30	32
	Guanine	2	33	–	23	43
	Hypoxanthine	2	37	–	20	54
	Xanthine	2	58	–	18	98
Lamb, veal, and game (other than organs)	Adenine	7	15.5	1.28	10.0	19.4
	Guanine	7	12.7	1.84	6.0	20.7
	Hypoxanthine	7	78.3	4.61	65.3	100.8
	Xanthine	7	3.77	2.47	0.0	15.2
Legumes	Adenine	38	33.7	5.30	0.23	120
	Guanine	38	40.0	5.84	3.32	168
	Hypoxanthine	38	12.7	2.11	0.0	32.9
	Xanthine	38	12.7	2.70	0.0	64
Nuts and seeds	Adenine	1	13.6	–	–	–
	Guanine	1	13.8	–	–	–
	Hypoxanthine	1	2.3	–	–	–
	Xanthine	1	1.7	–	–	–
Pork organ products	Adenine	5	53.7	9.31	24.3	81.1
	Guanine	5	60.4	15.59	21.2	103
	Hypoxanthine	5	54.5	1.18	34.0	71
	Xanthine	5	29.8	18.24	0.0	82
Pork (other than organs)	Adenine	10	17.5	1.09	13.2	23.0
	Guanine	10	13.4	0.66	10.6	16.6
	Hypoxanthine	10	65.5	4.42	43.6	90.4
	Xanthine	10	0.0	0.0	0.0	0.0
Poultry organ products	Adenine	30	62.4	5.02	31.3	122
	Guanine	30	96.1	9.20	36.1	153
	Hypoxanthine	18	40.1	2.02	0	71
	Xanthine	18	14.5	5.41	2.3	138
Poultry (other than organs)	Adenine	335	22.4	0.22	13.0	48.6
	Guanine	335	27.5	0.22	11.6	43.8
	Hypoxanthine	335	80.6	1.85	22.2	131
	Xanthine	135	5.23	0.50	0.0	11.3
Sausages and luncheon meats	Adenine	10	13.1	2.09	6.8	25.7
	Guanine	10	11.8	2.69	4.5	30.2
	Hypoxanthine	10	47.0	7.69	15.0	92.1
	Xanthine	10	2.06	1.07	0.0	9.1
Soups and sauces	Adenine	11	7.05	1.88	0.0	18.3
	Guanine	11	26.0	11.16	0.0	113
	Hypoxanthine	11	112	56.18	0.5	657
	Xanthine	11	4.26	1.43	0.2	12.2
Sweets	Adenine	1	0.7	–	–	–
	Guanine	1	0.1	–	–	–
	Hypoxanthine	1	0.0	–	–	–
	Xanthine	1	0.0	–	–	–
Vegetables	Adenine	86	25.8	3.92	0.38	216
	Guanine	86	29.2	4.51	1.1	299
	Hypoxanthine	86	4.08	1.07	0.00	73.3
	Xanthine	86	1.62	0.22	0.00	10.7

(*continued on next page*)

Table 2 (*continued*)

Food Group	Nutrient Name	N	Mean	Standard Error of the Mean	Minimum	Maximum
Vegetarian meat, fish, and egg alternatives	Adenine	38	25.4	2.15	0	47.1
	Guanine	38	28.7	2.43	0.04	57.2
	Hypoxanthine	38	2.85	0.67	0	19.0
	Xanthine	38	0.38	0.70	0	2.42

comparing purine values for different forms of a food, such as for raw and cooked forms of the same food. This kind of comparison is valid only when paired raw and cooked samples from the same source are analytically measured, in order to best estimate values for these forms.

3.3. Purine contents in alcoholic beverages

Dietary purine contents were determined in fifteen kinds of alcoholic beverages (details are provided in Supplementary Material, Table S2). The descriptions are those that were provided in the source documents, which in many cases were general rather than specific, such as "wine" with no further details as to the type of wine. Beer, in general, contained higher amounts of both purine bases, as compared to non-alcoholic beverages, wine, and whiskey. Light beer brewed to lower alcohol concentration contained relatively lower amounts of adenine and hypoxanthine, compared to regular beer. Regular beer had an average of 1.63 mg/100 mL adenine and 0.96 mg/100 mL hypoxanthine while light beer had an average of 1.34 mg/100 mL adenine and 0.52 mg/100 mL hypoxanthine. These findings are consistent with results in epidemiological studies where beer was found to be the most influential in increasing the risk of gout (Choi et al., 2004b).

3.4. Purine contents in dietary supplements

Purine contents determined in 13 different types of dietary supplements are presented in the Supplementary Material, Table S3. The products varied widely in their contents of purines depending on the type of product. DNA/RNA, beer (brewer's) yeast and chlorella (green algae) were particularly rich sources. The amounts in some dietary supplements are considerable, particularly if taken frequently. It should be noted that in addition to these products that have been analyzed, a number of other products are on the market, which provide varying, but in some products fairly concentrated, amounts of purines. When dietary therapy is used for treating hyperuricemia, Kaneko et al. (2014) recommends that all sources of supplements high in purines should be avoided in diets.

A number of marketed dietary supplements apparently contain purines or purine-containing constituents as significant components. These include yeast and meat extracts as well as products marketed for increasing energy or for losing weight and which contain adenosine, adenosine triphosphate (ATP), or guanine triphosphate (GTP). The Dietary Supplement Label Database (DSLD) is a public use database containing over 85,000 labels of supplements sold in the United States (accessed at https://www.dsld.nlm.nih.gov/dsld/index.jsp). A quick search of DSLD found that all of the supplement product categories analyzed by Kaneko et al. (2014) (see Supplementary Material, Table S3) were in some way represented in DSLD with the ingredient found in the search fields "Product-Name" or "Anywhere-on-Label". For example, "Ingredient = Algae" yielded 62 "Product-Name" mentions and 1007 "Anywhere-on-Label" mentions; "Ingredient = Yeast" yielded 187 Product-Name mentions and 19,504 Anywhere-on-Label mentions; and "Ingredient = RNA" yielded 105 Product-Name mentions and 7,439 Anywhere-on-Label mentions. In addition, a scan of the World Wide Web revealed at least 24 products with purines, 6 with pyrimidines, over 100 with the word adenosine, and hundreds with the word yeast on the label. These cursory checks suggest that there are potentially thousands of purine-containing supplement products on the market and in use by the public, and also very possibly by individuals who need to restrict purine intake. The actual purine content of such supplements is generally not available nor is it required to be listed on the product label.

The efficacy of purine-containing dietary supplements is unclear, and evidence is weak regarding their beneficial role in health. Nevertheless, there is an absence of reports of adverse events in healthy

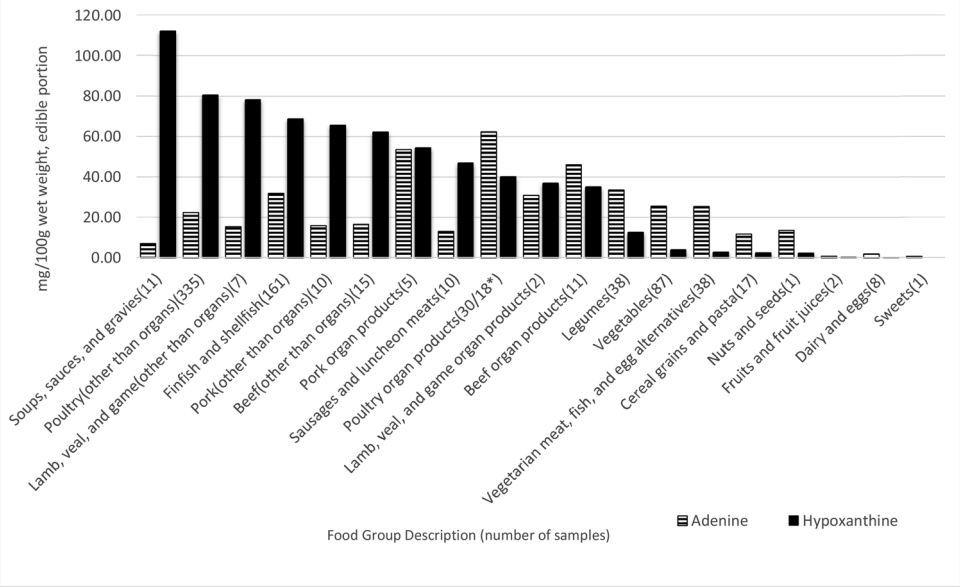

Fig. 3. Mean adenine and hypoxanthine levels in common food groups from published studies.
Footnote: *Poultry organ products number of samples: adenine = 30; hypoxanthine = 18.

people. The Natural Medicines Database, a commercially available database of dietary supplement monographs (accessed at https://naturalmedicines.therapeuticresearch.com), grades them as being likely safe supplements. However, among those who suffer from gout or kidney disease, this may not be the case, Dietary supplements are often very concentrated sources of ingredients, so data on dietary supplements as well as on food are critical to have in hand.

3.5. Data quality

The quality of each published resource in this study was initially scored using DQES, but the scoring process could not be completed, due to lack of standardized criteria for evaluating the analytical method of measuring purine. Each factor is briefly described below, and a summary of notable characteristics of each study is given in Table 1. Since the published reports obtained for this study did not comprehensively incorporate the factors that assure data quality, continued research is warranted.

3.5.1. Sampling plan

A good sampling plan takes into consideration the representativeness of samples. Ideally, samples should be collected from various regions, multiple cities per region, numbers of locations per city, different lots per location, and different seasons (Holden et al., 2002; Bhagwat et al., 2009). Samples in selected studies were collected from different sources and most were from countries other than the United States (Table 1). Even within the same country, regional differences in products can typically be observed. None of the studies in the present project had samples from multiple cities, locations, lots, or seasons. Therefore, relatively low scores were given for this criterion.

3.5.2. Sample handling

Homogenization is a critical step in purine analysis. Homogenization was performed in all studies in this project; however, not all homogenization processes were reported or validated in research reports. For example, two studies failed to report the methods or equipment that were used in sample homogenization (Kaneko et al., 2008; Qu et al., 2017). Other studies used different methods, such as a knife or blender, instead of a homogenizer. In addition, only a few studies reported moisture information. Moisture data are necessary for converting dry weight to wet weight when authors report purine contents on a dry weight basis. Proper sample storage is also critical to the overall accuracy. Most studies reported storing samples as either frozen or refrigerated before analysis.

3.5.3. Number of samples

The number of samples used for analysis are extremely important for accuracy of results. Analyzing multiple samples allows researchers to take both internal and external variations into consideration. Internal variations are mainly instrumental variations, which occur during the process of analysis. External variations refer to naturally occurring differences in foods, such as seasonality and soil condition. The impact of internal variations can also be minimized by doing multiple experiments on the same sample; however, the effect of external variations cannot be minimized without increasing the number of representative samples. Most studies enrolled in this project only had one sample but performed duplicates or triplicates. Therefore, only internal variations could be addressed in most studies.

3.5.4. Analytical methodology

Methods of analysis published are summarized in Table 1. However, this category could not be rated, because of a lack of accepted standardized analytical procedures for measuring purine, as previously mentioned. Analytical techniques have evolved in recent years, so the accuracy of analytical work has also improved. An expert review of methodology is needed to determine whether results generated prior to the 1990s are reasonably comparable to results determined more recently. Further research is needed in method development and subsequent lab analysis to obtain purine data. After standardized analytical methods are developed, the studies can be evaluated using the USDA DQES system.

3.5.5. Analytical quality control

Analytical quality control is necessary to ensure the accuracy and precision in performing analytical methods (Holden et al., 2002; Bhagwat et al., 2009). Accuracy is judged based on the results of certified, reference, and/or in-house control materials (Holden et al., 2002; Bhagwat et al., 2009). In-house materials are often used when certified reference materials for certain nutrients are not available and should be given a lower rating than certificated materials in the evaluation (Holden et al., 2002; Bhagwat et al., 2009). Precision is judged by the % coefficient of variation and the % recovery of the nutrient of interest after the processing of the sample (Bhagwat et al., 2009). Reference or in-house materials were used in about half of the studies in this project; however, the frequency of using quality control materials and results of assaying quality control materials were rarely reported. Thus, lack of information resulted in zero points for the respective rating characteristic, and consequently, overall low analytical quality control scores, for most references.

3.6. Limitations

Literature search was limited to the three prominent databases (Google Scholar, PubMed, and Scopus). Only data reported in English were included; reports written in other languages such as Japanese and German were found, but because of the language barrier, it was not possible to include those data in our dataset. A large number of food items reported in this paper were grown or produced outside the U.S.; thus their nutrient composition may vary from similar foods grown and produced in the U.S.

3.7. Future steps

No database for purine content in common US foods is publicly available, but such a database would be desirable, to support research and assist in developing preventive dietary guidance for at-risk individuals living in the U.S. A next step would be to conduct laboratory analysis of selected key foods in the United States (Haytowitz et al., 2002), given that most published works identified for this study were relatively old, lacked quality assurance information, and were predominantly from other countries. It would be important to determine the best analytical method or methods to use, to assess the availability of appropriate reference materials and, perhaps, to develop additional materials. Analyzing key foods could ensure that commonly consumed US products can be covered in the dataset. To ensure data quality, the plan would employ guidelines in the National Food and Nutrient Analysis Program (NFNAP) (Haytowitz and Pehrsson, 2018), including a multi-stage probability-proportional-to-size, nationally representative sampling plan, appropriate analytical methods, and a rigorous quality control program.

4. Conclusion

Gout is becoming a global burden at an increasing rate. Lifestyle and an overall healthy eating plan play an important role in supporting gout and hyperuricemia management. No database for purine content in common US foods is publicly available. While tables of purine content exist on the internet, they are poorly described and contain little or no information on the sources of data. Existing purine data from literature sources are limited and older, with the foods, analytical methods and quality control procedures poorly described in many cases. This literature overview illustrates the need for a high-quality nutrient

database on analytical purine values in commonly consumed US foods, alcoholic beverages and dietary supplements.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jfca.2019.103281.

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