Urine biomarker description

Amino acids

Biomarker	Biochemical, dietary, and health related information
Alanine	Alanine is classified as a nonpolar, aliphatic amino acid due to its hydrophobic nature and lack of charged functional groups in its side chain. It is one of the simplest amino acids in terms of chemical structure. While alanine itself may not be commonly used as a urinary biomarker in clinical practice, abnormalities in urinary amino acid profiles or ratios may provide valuable insights into metabolic disorders, renal function, or other physiological disturbances.
Glutamine	Glutamine is the most abundant amino acid in the human body and plays essential roles in protein synthesis, immune function, intestinal health, and nitrogen transport. While glutamine itself may not commonly be measured as a urinary biomarker, alterations in its urinary excretion can provide valuable insights into certain health conditions such as renal function, gastrointestinal disorders, and metabolic disorders.
Glycine	Glycine is a non-essential amino acid and as such not strictly required in the diet. It is abundant in protein-rich foods such as meat, fish, dairy products, and legumes. Glycine is involved in numerous physiological processes, including protein synthesis, bile acid conjugation, detoxification, and neurotransmission. It contributes to the maintenance of cellular structure and function and plays a crucial role in overall metabolic homeostasis. Alterations in urinary glycine levels may provide insights into certain metabolic and physiological processes.
Isoleucine	Isoleucine is one of the branched-chain amino acids (BCAAs), along with valine and leucine. Isoleucine is primarily obtained from dietary sources such as meat, fish, eggs, and dairy products, changes in dietary intake may influence urinary levels of isoleucine. Elevated urinary isoleucine levels are a diagnostic hallmark of Maple Syrup Urine Disease (MSUD) and can also indicate increased muscle protein breakdown, renal impairment, liver dysfunction, and metabolic disorders such as insulin resistance and diabetes. A study on people with type 1 diabetes found that isoleucine levels and other amino acids in urine were associated with risk for kidney disease progression and end-stage kidney disease (Mutter et al *Diabetologia*. 2022;65:140).
Leucine	Leucine is one of the branched-chain amino acids (BCAAs), along with valine and isoleucine. It is primarily derived from protein-rich foods such as meat, poultry, fish, eggs, dairy products, legumes, nuts, and seeds. In certain contexts, urinary levels of leucine may serve as a biomarker for assessing protein metabolism, muscle turnover, or certain metabolic disorders. Abnormalities in urinary leucine excretion may indicate alterations in protein intake, protein breakdown, or renal function.
Taurine	Taurine, also known as 2-aminoethanesulfonic acid, can be synthesized in the body from the amino acids cysteine and methionine, as well as through dietary intake. It is produced primarily in the liver via the cysteine sulfinic acid pathway. Taurine is primarily excreted from the body through urine after being metabolized or eliminated unchanged. The amount of taurine excreted in urine can be influenced by factors such as taurine intake from diet, endogenous synthesis, and renal function. Taurine is found in various foods, particularly meat, seafood, and dairy products. Individuals with diets rich in these sources of taurine may excrete higher levels of taurine in their urine compared to those with lower dietary intake.
Threonine	Threonine is an essential amino acid, meaning the body cannot produce it on its own and it must be obtained from the diet. Sources of threonine include many protein-rich foods such as meat, poultry, fish, dairy products, eggs, nuts, seeds, and legumes. Threonine metabolism involves several pathways in the liver and changes in threonine levels in urine can reflect alterations in liver function or metabolism. Monitoring threonine levels in urine can provide insights into an individual's nutritional status and dietary habits. Threonine and other amino acids in urine were reported to be associated with risk for kidney disease progression and end-stage kidney disease in people with type 1 diabetes (Mutter et al *Diabetologia*. 2022;65:140).

Amino acids (continued)

Biomarker	Biochemical, dietary, and health related information
Tryptophan	Tryptophan is an essential amino acid, meaning it cannot be synthesized by the body and must be obtained from the diet. Tryptophan is found in a variety of protein-rich foods such as poultry, meat, fish, eggs, dairy products, nuts, seeds, and legumes. It is also present in smaller amounts in certain plant-based sources like bananas, oats, and chocolate. Tryptophan serves as a precursor for the synthesis of various important molecules in the body, including serotonin, melatonin, and niacin (vitamin B3). Abnormalities in urinary tryptophan levels may be observed in certain metabolic disorders or medical conditions affecting tryptophan metabolism.
Tyrosine	Tyrosine is an α-amino acid and it has a side chain consisting of a benzene ring substituted with a hydroxyl group (-OH), making it a polar, aromatic amino acid. Tyrosine is a semi-essential amino acid, meaning it can be synthesized by the body from the essential amino acid phenylalanine through a biochemical pathway known as phenylalanine hydroxylase. However, dietary intake of tyrosine-rich foods such as meat, poultry, fish, dairy products, nuts, seeds, and certain grains can also contribute to tyrosine levels in the body. Tyrosine and its metabolites in urine serve as important markers for assessing liver and kidney function, and evaluating nutritional status. Measurement of urinary tyrosine levels may be relevant in the diagnosis and management of disorders affecting tyrosine metabolism, such as tyrosinemia or phenylketonuria (PKU).
Valine	Valine is one of the branched-chain amino acids (BCAAs), along with leucine and isoleucine. These amino acids are metabolized primarily in skeletal muscle tissue, where they serve as substrates for energy production through the tricarboxylic acid (TCA) cycle. The levels of valine in urine can vary depending on several factors, including dietary intake, metabolism, and overall health status. Generally, valine is typically excreted only in small amounts in urine under normal physiological conditions because it is primarily metabolized and utilized by the body for protein synthesis and energy production rather than excreted. Valine and other amino acids in urine were associated with risk for kidney disease progression and end-stage kidney disease in people with type 1 diabetes (Mutter et al *Diabetologia*. 2022;65:140).

Amino acid metabolism

Biomarker	Biochemical, dietary, and health related information
2-Hydroxyisobutyrate	2-Hydroxyisobutyrate (2-HIB) is a hydroxy acid, with the chemical formula $C_4H_8O_3$. 2-Hydroxyisobutyrate is produced as an intermediate in various metabolic pathways, including the catabolism of branched-chain amino acids (BCAAs) such as valine, leucine, and isoleucine. It is also formed during the metabolism of certain xenobiotics and environmental toxins. Elevated levels of 2-Hydroxyisobutyrate in urine have been reported in various pathological conditions, including inborn errors of metabolism, mitochondrial disorders, liver diseases, and certain types of cancer.
3-Hydroxyisobutyrate	3-Hydroxyisobutyrate (3-HIB) is an intermediary metabolite in the catabolism of the branched-chain amino acid valine. It plays a crucial role in energy metabolism by modulating lipid uptake and storage in muscle and adipose tissue, and its elevated levels are linked to insulin resistance and diabetes. Additionally, 3-HIB contributes to ATP production, especially under metabolic stress conditions. It is produced endogenously in the body as a metabolic intermediate in several pathways, including valine metabolism, thymine catabolism, and fatty acid oxidation. Urinary 3-HIB may serve as a biomarker for metabolic disorders, kidney function, oxidative stress, and nutritional status.
3-Hydroxyisovalerate	3-Hydroxyisovalerate is a hydroxy acid with a chemical structure derived from isovaleric acid, a short-chain fatty acid. It has a hydroxyl group (-OH) attached to the carbon adjacent to the carboxyl group (-COOH) on the isovalerate moiety. 3-Hydroxyisovalerate is produced as an intermediate in the catabolism of branched-chain amino acids (BCAAs), particularly leucine. When BCAAs are broken down for energy, 3-hydroxyisovalerate is formed as part of the process.
4-Deoxyerythronate	4-Deoxyerythronate, also known as 4-Deoxyerythronic acid, is a derivative of erythrose, a four-carbon sugar, with a hydroxyl group (-OH) replaced by a hydrogen atom on the fourth carbon. It is related to 4-deoxythreonate, and both are involved in the catabolism of the amino acid L-threonine. Threonine undergoes enzymatic reactions that break it down into various metabolites, including 4-deoxyerythronate. This production is part of the broader metabolic pathways that manage amino acid utilization and recycling, crucial for maintaining the body's nitrogen balance and energy production.

Amino acid metabolism (continued)

Biomarker	Biochemical, dietary, and health related information
4-Deoxythreonate	4-Deoxythreonate, also known as 4-deoxythreonic acid, is a byproduct of the catabolism of L-threonine, an essential amino acid. It belongs to the biochemical class of sugar acids and derivatives, along with 4-deoxyerythronate. These compounds contain a saccharide unit that bears a carboxylic acid group. 4-Deoxythreonate is a metabolite that has been implicated in oxidative stress and inflammation. Elevated levels of 4-deoxythreonate in urine may indicate increased oxidative stress and damage to cellular components, as well as inflammation within the body.
Ethanolamine	Ethanolamine is related to several amino acids, particularly through its role in metabolic pathways of serine. Serine can be enzymatically converted to ethanolamine in the presence of adequate levels of vitamin B6. In addition, ethanolamine is found naturally in various biological systems, where it serves as a precursor for the synthesis of phospholipids, such as phosphatidylethanolamine (PE), which are essential components of cell membranes. Changes in urinary ethanolamine levels may indicate alterations in phospholipid metabolism, neurotransmitter synthesis, or liver function. For example, elevated urinary ethanolamine levels have been reported in liver diseases such as hepatocellular carcinoma and cirrhosis.
Glycolate	Glycolate, also known as glycolic acid, is a small alpha-hydroxy acid (AHA) with the chemical formula $C_2H_4O_3$. Glycolate can be converted to glyoxylate, which plays a role in the glyoxylate cycle. This cycle is crucial for the metabolism of certain amino acids and the production of intermediates that can enter the citric acid cycle. Glycolate has been investigated as a potential urinary biomarker for certain metabolic disorders, particularly disorders of glyoxylate metabolism such as primary hyperoxaluria (PH) and related conditions. In these disorders, there is an abnormal accumulation of glyoxylate and oxalate, leading to the formation of kidney stones and renal damage. Glycolate is a significant toxic metabolite in ethylene glycol poisoning. Ethylene glycol is metabolized to glycolic acid, which is then further metabolized to oxalic acid, contributing to metabolic acidosis and renal toxicity.
Hippurate	Hippurate, also known as hippuric acid, is a metabolite formed by the conjugation of benzoic acid with glycine in a process known as glycine conjugation. Hippurate is found in various biological fluids, including urine, blood, and saliva. It is one of the major urinary metabolites excreted by humans and animals. Hippurate is also present in certain foods, particularly plant-based foods such as fruits, vegetables, and grains, which contain benzoic acid derivatives. Hippurate serves as a biomarker for various physiological and environmental factors. Changes in urinary hippurate levels may reflect alterations in dietary intake, gut microbiota composition, drug metabolism, and liver function. High urinary hippurate levels have been associated with increased consumption of plant-based foods rich in benzoic acid derivatives, while low levels may indicate alterations in liver function or drug metabolism.
Pyroglutamate	Pyroglutamate, also known as 5-oxoproline or pyroglutamic acid, is a naturally occurring compound that serves various biological functions in the body. Pyroglutamate can be converted back to glutamate by the enzyme 5-oxoprolinase. This conversion is essential for maintaining the balance of glutamate and glutamine in the body. This helps modulating the availability of glutamate, which is a key neurotransmitter and a precursor for other amino acids. Furthermore, pyroglutamate is an intermediate in the gamma-glutamyl cycle, which is crucial for the synthesis and recycling of glutathion. Pyroglutamate can be obtained from dietary sources, particularly protein-rich foods such as meat, fish, dairy products, and grains. It is also naturally present in certain fruits and vegetables, including avocado, spinach, and soybeans. Abnormal levels of pyroglutamate in the body may be associated with certain medical conditions or metabolic disorders. For example, elevated levels of pyroglutamate in urine is associated with increased risk for end-stage kidney disease in people with type 1 diabetes (Mutter et al *Diabetologia*. 2022;65:140).
Urea	Urea is a nitrogenous waste product formed in the liver through the breakdown of proteins and amino acids. Urea is present in the blood and bodily fluids of animals and humans as a waste product of protein metabolism. It is synthesized in the liver through the urea cycle, a series of biochemical reactions that convert ammonia (a toxic byproduct of protein metabolism) into urea, which is less toxic and more easily excreted. The majority of urea produced in the body is excreted by the kidneys into urine. The concentration of urea in urine can vary depending on factors such as hydration status, dietary protein intake, renal function, and metabolic rate. Higher dietary protein intake typically leads to increased urea production and excretion in urine, while dehydration or kidney dysfunction may result in more concentrated urine and higher urea concentrations.

Dietary Metabolites

Biomarker	Biochemical, dietary, and health related information
2-Furoylglycine	2-Furoylglycine, also known as pyromellitic acid monoamide, is a urinary metabolite derived from the metabolism of furan-containing compounds in the body. Elevated levels of 2-furoylglycine in urine may indicate increased exposure to furan compounds, which can occur through dietary intake of certain foods (e.g., coffee, canned foods) or occupational and environmental exposures. Furan compounds have been classified as potential human carcinogens, and their consumption has been associated with adverse health effects. Therefore, monitoring urinary levels of 2-furoylglycine may have implications for assessing exposure to furan compounds and evaluating associated health risks.
Arabinose	Urinary arabinose levels have attracted interest in nutritional and medical research due to their potential as biomarkers for dietary intake and health status. Arabinose, a pentose sugar, is not synthesized by the human body but is obtained mainly through the diet, particularly from the consumption of plant-based foods that contain polysaccharides and fibers rich in arabinose residues. Arabinose can be an indicator of Plant Consumption: Elevated levels of urinary arabinose can be indicative of a diet rich in whole plant foods. As such, urinary arabinose has been explored as a non-invasive biomarker for dietary fiber intake or adherence to diets high in fruits, vegetables, and whole grains.
Ethanol	Ethanol is primarily metabolized in the liver by the enzyme alcohol dehydrogenase (ADH) and other enzymes, including aldehyde dehydrogenase (ALDH). These enzymes convert ethanol into acetaldehyde, which is further metabolized into acetic acid and then into carbon dioxide and water. Ethanol metabolism produces energy but also generates toxic byproducts such as acetaldehyde, which can contribute to tissue damage and alcohol-related health problems. Ethanol and its metabolites can be detected in urine following consumption of alcoholic beverages or exposure to ethanol-containing products. Ethanol itself is rapidly eliminated from the body through urine, breath, and sweat, with approximately 5-10% being excreted unchanged in urine. However, ethanol is not commonly used as a biomarker in urine due to its short half-life and the availability of more specific and sensitive biomarkers for alcohol consumption. Ethanol can occasionally be observed at unphysiologically high concentrations in urine due to disinfectant contaminations from sample collection processes and/or due to contamination in air from lab handling, such as cleaning of well-plates.
Mannitol	Mannitol is a type of sugar alcohol used as a low calorie sweetener as it is poorly absorbed by the intestines. As a medication, it is used to decrease pressure in the eyes, as in glaucoma, and to lower increased intracranial pressure. Mannitol is naturally occurring in various foods, including fruits and vegetables, seaweed, mushrooms, and processed foods. When consumed, mannitol is poorly absorbed in the intestines and is largely excreted unchanged in urine. While mannitol itself may not be considered a traditional urinary biomarker, its urinary excretion can provide valuable information about physiological processes and certain medical conditions such as acute kidney injury (AKI), and glomerular filtration rate.
Proline betaine	Proline betaine, also known as stachydrine, is a naturally occurring compound found in various plant foods, particularly citrus fruits. Its presence in urine is a direct reflection of recent dietary intake, making it a reliable marker for citrus fruit consumption. Studies have suggested that higher intake of citrus fruits, reflected by elevated proline betaine levels, is associated with better metabolic health markers, such as improved insulin sensitivity and reduced risk of metabolic syndrome.
Propylene glycol	Propylene glycol is a synthetic organic compound that belongs to the alcohol family, specifically a diol (or glycol). Propylene glycol is commonly used in various consumer products, including foods, cosmetics, pharmaceuticals, and e-cigarette liquids, among others. Consequently, it can be detected in biological fluids such as urine following exposure through ingestion, inhalation, or dermal absorption. It cannot be produced de novo in human metabolism. Once ingested, it is metabolized in the liver into pyruvic acid, lactic acid, and acetic acid, which are then utilized in various metabolic pathways. For example, propylene glycol can be converted into glucose via gluconeogenesis, which helps maintain blood sugar levels and provides energy, especially during periods of fasting or intense physical activity.
Quinate	Quinate, also known as quinic acid or 3-dehydroshikimic acid, is a naturally occurring compound found in various plants, fruits, and beverages. In humans, quinic acid is metabolized by gut microbiota in the colon. It undergoes bacterial degradation to form various metabolites, including other organic acids such as shikimic acid and benzoic acid. Quinic acid exhibits various biological activities and has been studied for its potential health benefits. Elevated levels in urine can be due to dietary intake, metabolic disorders, gut micorbiota composition, liver and kidney dysfunction, medication and supplements.
Sucrose	Sucrose is a disaccharide composed of one molecule of glucose and one molecule of fructose linked by a glycosidic bond. Dietary origins include table sugar, fruits and vegetables, honey and syrup, as well as soft drinks, candies, cereals, and baked goods. Sucrose is not typically found in high concentrations in urine because it is efficiently broken down and absorbed in the small intestine by the enzyme sucrase. However, in certain conditions where there is impaired digestion or absorption of sucrose, such as sucrase-isomaltase deficiency (CSID), sucrose can appear in the urine.
Xylose	Xylose is a naturally occurring sugar classified as a monosaccharide of the aldopentose type, meaning it contains five carbon atoms and an aldehyde functional group. Xylose is metabolised by humans, although it is not a major human nutrient and is largely excreted by the kidneys. Humans can obtain xylose only from their diet, and the levels in urine originate primarily from dietary intake of foods containing xylose or its derivatives. This is mainly plant-based foods, including fruits and vegetables. It can also originate from sugar-free products and dietary supplements.

Energy metabolism

Biomarker	Biochemical, dietary, and health related information
Citrate	Citrate, also known as citric acid or tricarboxylic acid, is a key intermediate in cellular metabolism and a ubiquitous organic acid found in various biological systems. Urinary citrate serves as an important biomarker for kidney stone risk assessment, acid-base status, and bone health. Monitoring urinary citrate levels can aid in the diagnosis and management of kidney stone disease, metabolic disorders, and conditions affecting bone metabolism. It can also inform dietary and pharmacological interventions aimed at reducing the risk of kidney stones and maintaining overall health. Potassium citrate supplement may increase the citrate values in urine.
Glucose	Under normal physiological conditions, glucose is filtered by the kidneys but is almost entirely reabsorbed in the renal tubules, resulting in minimal glucose excretion in the urine. The renal threshold for glucose reabsorption is typically around 10 mmol/L for healthy individuals. When blood glucose levels exceed this threshold, glucose spills into the urine, resulting in glucosuria (the presence of glucose in the urine). Glucose is still detectable by NMR in almost all samples from general population cohorts, but the distribution tends to be vastly distinct from cohorts of people living with diabetes. Absolute glucose concentrations tend to be ~0.1-0.5 mmol/L in general population cohorts (Li, Ihanus et al, *Int J Epidemiol*. 2022;51:2022). In both settings, the distribution is often skewed and extreme outliers are common. Measurement of glucose levels in urine can be used as a diagnostic marker for diabetes mellitus and other glucose metabolism disorders.
Lactate	Lactate plays a key role in cellular metabolism, particularly under anaerobic conditions where it is produced from pyruvate during glycolysis to generate energy. It serves as a fuel source, a signaling molecule, and is involved in gluconeogenesis, inflammation regulation, and tissue repair. Elevated lactate concentrations in urine can indicate various metabolic disturbances. High levels may result from intense physical activity, certain dietary patterns (such as high carbohydrate intake), or underlying health conditions such as diabetes or kidney disease.
cis-Aconitate	Cis-aconitate, also known as cis-aconitic acid or simply cis-acid, is an organic compound belonging to the class of organic acids. It is primarily synthesized and utilized within cells as part of the tricarboxylic acid (TCA) cycle, where it serves as an intermediate in the conversion of citrate to isocitrate. As a metabolic intermediate, cis-aconitate does not readily cross cell membranes and is primarily metabolized within cells rather than excreted directly into urine. Therefore, its levels in urine are generally very low under normal physiological conditions.
trans-Aconitate	Trans-aconitate, also known as trans-aconitic acid, is an isomer of cis-aconitate, meaning they have the same molecular formula but different structural arrangements. Unlike cis-aconitate, trans-aconitate is not direct intermediate in the TCA but can be formed from cis-aconitate. Trans-aconitate is generally less common in humans compared to cis-aconitate. Trans-aconitate is found naturally in various fruits and vegetables, including apples, grapes, tomatoes, and potatoes.

Microbial metabolism

Biomarker	Biochemical, dietary, and health related information
3-Hydroxyhippurate	3-Hydroxyhippurate (3-HHA) is a metabolite found in urine, derived from the metabolism of certain aromatic compounds, particularly phenolic acids. It is formed by the conjugation of 3-hydroxybenzoic acid with glycine in the liver. It can also be produced as a product of the gut microbiota's metabolism of dietary aromatic compounds. Specifically, gut bacteria metabolize these compounds into benzoate, which is then conjugated with glycine in the liver to form hippurate and its derivatives, including 3-Hydroxyhippurate. Measurement of 3-hydroxyhippurate levels in urine can provide insights into the exposure to and metabolism of certain aromatic compounds in the body. Changes in urinary 3-hydroxyhippurate levels may be indicative of alterations in dietary intake, exposure to environmental toxins, or variations in metabolic pathways associated with phenolic compound metabolism. Consumption of foods rich in phenolic compounds, such as fruits, vegetables, nuts, seeds, and beverages like coffee, tea, and wine, can increase the urinary excretion of 3-hydroxyhippurate.
4-Hydroxyhippurate	4-Hydroxyhippurate is a metabolite derived from the intake of polyphenol-rich foods. It is particularly associated with the consumption of fruits, vegetables, and beverages such as tea and coffee. Gut microbiota plays a crucial role in the metabolism of dietary polyphenols, converting them into various metabolites, including 4-hydroxyhippurate. 4-Hydroxyhippurate serves as a valuable urinary biomarker for dietary polyphenol intake and gut microbiota activity. Its measurement provides insights into the consumption of polyphenol-rich foods and the overall antioxidant intake, which are important for nutritional and health assessments.

Microbial metabolism (continued)

Biomarker	Biochemical, dietary, and health related information
Acetate	Acetate is a short-chain fatty acid that is a byproduct of the digestion and fermentation of dietary fibers by gut bacteria, as well as the metabolism of certain amino acids and sugars. A diet high in these components can lead to increased acetate production. Additionally, the consumption of alcoholic beverages, which contain ethanol, can also result in elevated acetate levels after ethanol is metabolized. Therefore, variations in urine acetate levels can reflect changes in diet or alcohol intake.
Dimethylamine	The relationship between urinary Dimethylamine (DMA) levels and diet is rooted in the metabolism of dietary components by the gut microbiota and the body's processing of certain nutrients and compounds. DMA can be produced endogenously as a byproduct of the metabolism of certain dietary constituents, including choline, lecithin, and trimethylamine N-oxide (TMAO). The metabolic pathways involving these nutrients and the gut microbiota's role in converting dietary precursors into DMA highlight the link between diet, metabolic processes, and the composition of urinary metabolites.
Formate	Formate, also known as formic acid, is the simplest carboxylic acid with the chemical formula HCOOH. In the body, formate is primarily generated from the oxidation of formaldehyde by the enzyme formaldehyde dehydrogenase. Formate plays a crucial role in one-carbon metabolism, serving as a key intermediate in the synthesis of nucleotides and amino acids. It is produced in the mitochondria and cytosol from various substrates, including methanol, branched-chain fatty acids, and amino acids. Gut microbiota can produce formate through the fermentation of dietary fibers and other substrates. This formate can be absorbed into the bloodstream and subsequently excreted in the urine. Elevated formate concentrations in urine can also indicate excessive intake of methanol or certain amino acids, or metabolic disturbances such as folate deficiency. High urinary formate levels may also be associated with increased risk of metabolic disorders, including kidney dysfunction and certain types of cancer.
HPHPA: 3-(3-Hydroxyphenyl)-3-hydroxypropanate	3-(3-Hydroxyphenyl)-3-hydroxypropanate (HPHPA), also known as 3,4-dihydroxyphenylpropionic acid, is a metabolite derived from the microbial metabolism of polyphenols in the gut. In urine it can serve as a biomarker for dietary intake of polyphenols, particularly flavonoids, and gut microbial activity. It may be used as a biomarker for the health effects of polyphenol-rich diets or interventions targeting gut microbiota.
Indoxyl sulfate	Indoxyl sulfate is a metabolite formed in the liver through the sulfation of indole, which is produced by the bacterial fermentation of dietary tryptophan in the gut. Indoxyl sulfate is considered a uremic toxin, meaning its accumulation in the body can contribute to the progression of kidney disease and associated complications. Elevated levels of indoxyl sulfate in urine and blood are associated with the progression of chronic kidney disease and increased cardiovascular risk.
Trimethylamine N-oxide	Trimethylamine-N-oxide (TMAO) is a small organic compound that is formed in the liver as a metabolite of trimethylamine (TMA), which is produced by gut bacteria during the digestion of certain nutrients, such as choline, carnitine, and betaine. Elevated levels of TMAO in blood and urine have been linked to certain medical conditions, including cardiovascular disease, atherosclerosis, and kidney dysfunction. Dietary intake of choline, carnitine, and betaine-rich foods can contribute to increased TMAO production in the body. Foods such as red meat, eggs, fish, and dairy products are sources of these nutrients and can lead to higher TMAO levels when consumed in large quantities.

Nicotinate and nicotinamide metabolism

Biomarker	Biochemical, dietary, and health related information
1-Methylnicotinamide	1-Methylnicotinamide (1-MNA) is a methylated derivative of nicotinamide (vitamin B3 or niacinamide). Alterations in 1-MNA levels in urine have been associated with various metabolic disorders, including obesity, diabetes, and metabolic syndrome. Changes in niacin metabolism and 1-MNA excretion may reflect dysregulation of metabolic pathways and metabolic dysfunction. Studies have suggested a potential link between increased 1-MNA levels and cardiovascular health, certain cancers, and metabolic disorders.

Nicotinate and nicotinamide metabolism (continued)

Biomarker	Biochemical, dietary, and health related information
Trigonelline	Trigonelline is an alkaloid with chemical formula $C_7H_7NO_2$. It is the methylated derivative of niacin, an essential vitamer of vitamin B3. It is formed in the broader metabolism of niacin, an essential process for the production of NAD+. Trigonelline has been studied for its potential health benefits and biological activities. It exhibits antioxidant, anti-inflammatory, and neuroprotective properties, which may contribute to its protective effects against oxidative stress and neurodegenerative diseases. Trigonelline has also been investigated for its role in modulating glucose metabolism and insulin sensitivity. Trigonelline is a natural alkaloid compound found in various plants, including fenugreek seeds (Trigonella foenum- graecum), coffee beans, and certain legumes.

Nucleotide metabolism

Biomarker	Biochemical, dietary, and health related information
3-Aminoisobutyrate	3-Aminoisobutyrate (3-AIB) is a non-proteinogenic amino acid, meaning it is not incorporated into proteins during translation. It is also known as β-aminoisobutyric acid or β-AIB. It is primarily involved in the catabolism of thymine, a component of DNA. During this process, 3-Aminoisobutyrate is converted to 2-methyl-3-oxopropanoate by the enzyme D-3-aminoisobutyrate-pyruvate aminotransferase. 3-Aminoisobutyrate has been shown to induce the browning of white fat cells, which can enhance energy expenditure and improve metabolic health. 3-Aminoisobutyrate is a product of thymine metabolism within the body and not directly obtained from food. However, its levels can be influenced by factors such as exercise, which boosts its production in skeletal muscle.
Allantoin	Allantoin is also known as 5-ureidohydantoin or glyoxyldiureide, and its molecular formula is $C_4H_6N_4O_3$. In humans, allantoin is produced through the non-enzymatic oxidation of uric acid by reactive oxygen species. This process occurs because humans lack the enzyme urate oxidase (uricase), which is responsible for converting uric acid to allantoin in many other mammals. As a result, allantoin serves as a biomarker for oxidative stress in the human body. It is also used as a measure of the body's antioxidant capacity, indicating how well the body can neutralize free radicals. Changes in allantoin levels can be related to diet, health status, and exposure to environmental stressors.
Hypoxanthine	Hypoxanthine is a naturally occurring purine derivative and an intermediate in the synthesis and breakdown of purine nucleotides. Measurement of hypoxanthine levels in biological fluids, such as blood or urine, can provide valuable diagnostic information in various medical conditions. Elevated levels of hypoxanthine may indicate increased purine breakdown, as seen in disorders such as gout, Lesch-Nyhan syndrome, or certain metabolic disorders. Conversely, low levels of hypoxanthine may be observed in conditions affecting purine metabolism or salvage pathways.
Pseudouridine	Pseudouridine plays important roles in RNA structure, stability, and function. Pseudouridine is formed post-transcriptionally by the action of pseudouridine synthase enzymes, which isomerize uridine to pseudouridine in RNA molecules. Since pseudouridine cannot be reused by the body, it is excreted unchanged in the urine. Thus, urinary levels of pseudouridine directly reflect its turnover and the overall RNA degradation process. Pseudouridine serves as an important urinary biomarker due to its stable excretion and direct reflection of RNA turnover. Elevated levels in urine can indicate various conditions, including cancers, autoimmune diseases, liver diseases, and renal function impairment.
Uracil	Uracil is one of the four nucleobases found in the nucleic acid RNA (ribonucleic acid). Uracil is synthesized in the body through various metabolic pathways, including the de novo synthesis pathway and the salvage pathway. It can be further metabolized or incorporated into RNA molecules during RNA synthesis. Excess uracil or breakdown products may be excreted from the body through urine. Under normal physiological conditions, uracil is typically not excreted in significant quantities in urine. However, changes in urinary uracil levels may occur in certain metabolic disorders, genetic conditions, or diseases affecting nucleotide metabolism or RNA turnover.
Xanthosine	Xanthosine is a naturally occurring nucleoside, composed of a nitrogenous base (xanthine) and a sugar (ribose). It is a precursor in the metabolism of nucleic acids, particularly in the purine salvage pathway, where it can be converted into other important compounds such as guanosine monophosphate (GMP). Its involvement in purine metabolism pathways suggests that alterations in its urinary excretion could be indicative of underlying metabolic or renal dysfunction.

Urine volume scaling factor

Biomarker	Biochemical, dietary, and health related information
Creatinine	Creatinine is a waste product generated from the breakdown of creatine phosphate, a molecule found in muscle tissue. It is produced at a relatively constant rate in the body, primarily by skeletal muscles, and is excreted by the kidneys into urine. Creatinine is present in urine at relatively constant levels, reflecting muscle metabolism and renal function. The concentration of creatinine in urine is influenced by factors such as muscle mass, age, gender, and hydration status. In healthy individuals, urinary creatinine excretion rates remain stable over time. Urinary creatinine levels are often used to normalize the concentrations of other urinary analytes, such as proteins or metabolites, to account for variations in urine concentration due to hydration status and kidney function. Creatinine normalization helps standardize urinary analyte measurements and improve the accuracy of diagnostic tests. The influence of alternative scaling methods of urine biomarkers in epidemiological research is discussed in detail by Li et al, Characteristics of normalization methods in quantitative urinary metabolomics – implications for epidemiological applications and interpretations. *Biomolecules*. 2022; 12(7):903.