# The Utilization of Urine Processing for the Advancement of Life Support Technologies

Elysse N. Grossi[1]
*University of California Santa Cruz, University Associated Research Center*
*NASA Ames Research Center, Moffett Field, CA 94035*

*and*

John A. Hogan[2] and Michael Flynn[3]
*NASA Ames Research Center, Moffett Field, CA 94035*

**The success of long-duration missions will depend on resource recovery and the self-sustainability of life support technologies. Current technologies used on the International Space Station (ISS) utilize chemical and mechanical processes, such as filtration, to recover potable water from urine produced by crewmembers. Such technologies have significantly reduced the need for water resupply through closed-loop resource recovery and recycling. Harvesting the important components of urine requires selectivity, whether through the use of membranes or other physical barriers, or by chemical or biological processes. Given the chemical composition of urine, the downstream benefits of urine processing for resource recovery will be critical for many aspects of life support, such as food production and the synthesis of biofuels. This paper discusses the beneficial components of urine and their potential applications, and the challenges associated with using urine for nutrient recycling for space application.**

## Nomenclature

| | | |
|---|---|---|
| *ATP* | = | adenosine triphosphate |
| *BW* | = | black water |
| $CO_2$ | = | carbon dioxide |
| *GAA* | = | guanidoacetic acid |
| $H_2S$ | = | hydrogen sulfide |
| *ISS* | = | International Space Station |
| *kg/CM-d* | = | kilograms of waste produced per crewmember per day |
| *TMAO* | = | trimethylamine N-oxide |

[1] Synthetic Biology Development Engineer and Researcher, Bioengineering Branch, M/S 239-15, Moffett Field, CA 94035
[2] Primary Investigator, Bioengineering Branch, M/S 239-15, Moffett Field, CA 94035.
[3] Primary Investigator, Bioengineering Branch, M/S 239-15, Moffett Field, CA 94035.

## I. Introduction

Long duration space exploration missions pose new challenges for life support technologies in regards to durability, maintenance needs, resupply requirements, and overall self-sustainability. All earth-based support used for resupply will be rendered unusable due to the distance and complexity of travel for long duration missions. Deep space missions will have strict upmass requirements, especially concerning weight and physical space for the storage of all supplies, including those serving basic life support functions. Due to the independence of proposed future space travel, technologies supporting crewmember livelihood and health monitoring will need to rely on resource recovery and self-sustainability.

The production of wastes is unavoidable during manned missions. The most common wastes produced during manned missions include solids wastes, such as packaging and other trash, liquid wastes, including urine, feces water and hygiene water, and respiratory wastes, such as carbon dioxide ($CO_2$). While solid wastes are harder to recover resources from, the physical space required to store solid wastes can become an issue during spaceflight. Technologies to process solid wastes include compacting and heating to recover any excess water. Respiratory wastes are primarily comprised of $CO_2$, but also include small droplets of saliva or water, which can be recovered and processed, as well. Unlike the threat of accumulating wastes impinging on limited space, the uncontrolled accumulation of respiratory wastes can alter the humidity and oxygen concentrations, quickly creating an inhospitable environment for crewmembers.

Liquid human wastes present a unique opportunity for resource recovery. Defecation and micturition, also known as urination, are the most efficient methods of removing wastes and contaminants from the body[1]. Wastes are secreted and expelled from the body in order to maintain homeostatic balance. This is achieved by removing contaminants and unused or unnecessary biomass and nutrients, such as vitamins, minerals, and therapeutics[1]. Waste contents are directly related to an individual's diet, overall health, hydration levels, use of medications or supplements, and exposure to environmental toxins, such as pollution and radiation. The feasibility of resource recovery from specific waste streams is determined by the concentrations of vital nutrients and compounds that are readily available. For example, recovery of water from urine, feces and other hygienic wastes is highly dependent on the hydration levels of the individual producing the wastes. As a person becomes dehydrated, the wastes that are produced contain a high concentration of undissolved solids in smaller volumes of water, making it harder to remove the wastes from the body. Given the controlled nature of crewmembers' diets[2], it is reasonable to assume which valuable resources will be available for recovery through waste processing.

Of the wastes produced during manned missions, water-based hygiene wastes, primarily urine, show the strongest potential for resource recovery. Logistically, it is cleaner, safer and more efficient to work with liquid wastes that can be easily pumped from toilets to the waste processing system. Additionally, recovering resources from liquid hygiene wastes gives direct access to larger volumes of concentrated compounds and molecules that could be reused for further life support practices. According to data collected from prior missions, the total kilograms of urine wastes, solid (dry basis) and liquid (water), produced by crewmember per day are more than that produced in fecal wastes[2] (Table 1). Table 1 illustrates the specific values reported for both solid wastes and water wastes produced by crewmember per day[2], with total urine wastes (1.945 kg/CM-d) weighing more than fifteen times the amount produced by feces (0.123 kg/CM-d). Recovering only water from urine wastes allows for total urine wastes to be reduced, theoretically, by 97%, assuming 100% recovery is achievable.

**Table 1. Average Values of Wastes Produced Per Crewmember Per Day (kg/CM-d)**

| Wastestream | Solid Waste (dry basis) | Water Waste (liquid) |
|---|---|---|
| Feces | 0.032 kg/CM-d | 0.091 kg/CM-d |
| Urine | 0.059 kg/CM-d | 1.886 kg/CM-d |

Another factor that requires consideration for resource recovery and life support systems is the feasible usage of recovered materials and resources. Desired resources are either directly integral components of life support systems, such as oxygen and potable water, therapeutics, or are fundamental building block molecules and compounds that can be used to synthesize products downstream. The range of potentially harvestable compounds and materials from urine is broad, making it a valuable option for resource recovery. In addition to the beneficial contents of urine, total recycling of urine wastes through the recovery of water, as well as solutes and compounds, will dramatically reduce the need for waste storage[3]. This paper will not discuss physical processing methods for resource recovery, but will instead focus on the potential applications for beneficial compounds that may be recovered from urine wastes during long duration space exploration.

## II. Urine Composition

Urine has been used as a diagnostic indicator of an individual's overall health for thousands of years[1,4], and has made the complete composition of urine a topic of interest amongst health professionals and the research community. Physical examination of urine defines the color, odor, clarity, volume, and specific gravity of suspended solids[4]. Colorimetric analysis is a good indicator of hydration levels. Frequency of urination can illustrate irritation, infection, or blockage of the urinary tract. In depth chemical analyses of urine allow for specific compounds to be detected, and can determine the health of specific organs or the uptake of medications. Chemical analysis of urine illustrates the presence and specific concentrations of proteins, blood cells, glucose, bilirubin, urobilinogen, ketone bodies, nitrites, leukocyte esterase, or changes in pH levels[4]. The presence of some chemicals and metabolic byproducts are normal, whereas some can indicate disease. Glucose in the urine, especially in high concentrations, can be an indicator of diabetes[4]. The presence of blood cells and bacterial byproducts can be an indication of infection. Determining a compendium of concentration standards and normalities for urine contents is an integral part of expanding the diagnostic capabilities of urinalysis[1]. Yet, determining a complete list of urine contents is also important for identifying potential avenues for resource recovery during spaceflight.

Separating urine from black water (BW), which is a mixture of urine and feces wastes, can reduce the presence of pathogens and result in a high nutrient-containing wastestream[5]. Standard compounds found in normal urine samples include cations, anions, inorganic salts, and byproducts from physiological processes[1-6]. It's estimated that the average person on earth produces 1.5 liters of urine per day (24 hours), with the acceptable range extending from 0.6 liters to 2.0 liters[4]. The presence of such compounds and molecules can fluctuate due to the unstable nature of urine after it leaves the body[1,4]. Bacterial growth can contribute to the decomposition of urine[1], influencing a change in pH to be more alkaline and the breakdown of urea, which releases ammonia[4].

Superclassification of chemicals and trace compounds identified in previous studies[1,3-6] give an overview of the thousands of metabolites available in human urine. Superclasses include aliphatic compounds, alkaloids and their derivatives, amino acids and peptides, aromatic compounds, carbohydrates and carbohydrate conjugates, metal compounds, non-metal compounds, mixed metal and non-metal compounds, lignans and norlignans, lipids, nucleotides and nucleosides, organic acids, organic halides and organometallic compounds, organophosphorus compounds, polyketides, and tannins[1]. Given the uneven distribution of the number of compounds identified per superclass, only the major contributing superclasses and their highly represented compounds are considered for resource recovery in this review. The compound and metabolite concentration data used to support the potential avenues for resource recovery are primarily based on the findings of Bouatra, *et al.* (2013)[1]. Bouatra, *et al.* compared a compendium of previously published concentration values while using a number of advanced techniques to fully characterize the presence of urine metabolites. All metabolite concentrations reported were normalized to the sample's creatine concentration, reported as μM/mM or mM/mM creatine, for normalization[1]. A summarization of the following compounds can be found in Table 2.

### A. Aliphatic Compounds

Aliphatic compounds are compounds that are primarily comprised of carbon and hydrogen that are non-aromatic, meaning they do not contain aromatic rings. Structurally, aliphatic compounds can be represented as straight or branched chains, or non-aromatic rings. The aliphatic compound superclass can be divided into three subclasses that include aliphatic acyclic compounds, aliphatic homomonocyclic compounds, and aliphatic heteromonocyclic compounds.

*1. Aliphatic acyclic compounds*

Aliphatic acyclic compounds can be distinguished by the structural presence of non-aromatic rings. Of the 93 compounds previously reported within the aliphatic acyclic compounds superclass, five compounds are detectable in urine with a 100% occurrence rate.

Dimethylamine ($C_2H_7N$) is a secondary amine[7] that is found in many plant and animal-based foods, specifically fish and seafoods[8,9]. Concentrations of dimethylamine in human urine can fluctuate with changes to diet[8]. The reaction between methanol and ammonia in the presence of a dehydration catalyst can produce dimethylamine[7,9]. The average concentration of dimethylamine isolated from urine samples has been reported as 30.8 μM/mM creatine, with a maximum reported concentration of 59.2 μM/mM creatine[1]. Dimethylamine as a pure chemical substance has many industrial applications, as it is a common component in soaps, cleaning compounds, and agricultural fungicides[1,7-9]. For aerospace applications, dimethylamine salt can be combined with sodium nitrate to produce dimethylnitrosamine. Reducing dimethylnitrosamine with zinc, or oxidation with chloramine, will produce 1,1-dimethylhydrazine, which is commonly used for the production of rocket fuel[8,9].

Ethanolamine ($C_2H_7NO$) is a hygroscopic amino alcohol and an abundant head group for phospholipids, which are a critical component of biological, lipid bilayer membranes[10-12]. Given the amino alcohol structure, ethanolamines are also used to describe a structural class of antihistimines, including carbinoxamine, clemastine, dimenhydrinate, diphenhydramine, and doxylamine[11]. Average reported concentrations of ethanolamine from urine samples were reported as 37.0 μM/mM creatine, with a maximum detected value of 56.2 μM/mM creatine[1]. Ethanolamine has many industrial applications that would be of interest for long duration mission applications, such as use as a surfactant, in gas scrubbing, specifically with $CO_2$ and $H_2S$, and in pharmaceutical formulation and synthesis[10,12].

Methanol ($CH_4O$), also referred to as methyl alcohol, represents alcohol in the simplest form[13,14], and is biologically produced via bacterial anaerobic metabolism. Prior to the analysis of Bouatra, *et al.*, methanol had not been reported as a metabolite or compound that could be isolated from human urine. Current reported concentrations of methanol from urine samples range from 10.0 μM/mM creatine to 117.0 μM/mM creatine, with an average of 37.0 μM/mM creatine[1]. Methanol can be oxidized to produce $CO_2$ and water. Methanol's representation as a polar liquid in room temperatures allows it to be used as fuel, solvent, and antifreeze solution in industrial applications[14]. Resource recovery of methanol could serve as a building block for the synthesis of a wide variety of products in space.

Trimethylamine N-oxide ($C_3H_9NO$), or TMAO, is a common metabolite in humans and animals, and is the main oxidation product of trimethylamine[15-17]. During metabolism, high concentrations of trimethylamine N-oxide, due to the presence of bacteria that convert dietary carnitine and lecithin into TMAO, can alter cholesterol metabolism in the intestines, liver and vascular walls[17,18]. Reported average concentrations of TMAO detected in urine samples are 91.0 μM/mM creatine, with a maximum detected value of 509.0 μM/mM creatine. Much like many of the compounds detected, diet and microbial health can influence levels of TMAO detected in the urine. While TMAO doesn't illustrate the industrial application of the previously discussed compounds, there are potential pharmaceutical applications. Targeted nitroxide agents, including TMAO, have shown success with preventing, mitigating and treating radiation injury, particularly in mitochondria[19].

Urea ($CH_4N_2O$) is a metabolite formed via the deamination of amino acids in the liver, and is abundant in urine[20,21]. Urea is the end product of protein catabolism in the urea cycle in the body. It is estimated that urea comprises approximately half of the total urinary solids[20], and 90-95% of the total nitrogen in urine[6]. Reported concentrations of urea detected in urine samples average 12,285 μM/mM creatine, with a maximum detected value of 49,097 μM/mM creatine[1]. The high levels expelled in urine illustrate the lack of physiological function for urea. Urea decomposes rapidly during storage, converting primarily to ammoniacal nitrogen[6]. Taking the high concentration of urea in urine, with 100% occurrence, into consideration, urea storage could be utilized for nitrogen sequestration and reclamation during long duration missions. Downstream space applications include fuel supplementation, the synthesis of synthetic fertilizers for plant growth and crop production, and as a building block molecule for other product synthesis.

*2. Aliphatic homomonocyclic compounds*

While just 18 of the 3,079 compounds detected can be described as aliphatic homomonocylic compounds, only one chemical from the aliphatic homomonocyclic compounds superclass, myoinositol ($C_6H_{12}O_6$), is detectible with a 100% occurrence rate. Myoinositol is a cyclic polyalcohol and an isomer of glucose that plays a valuable role in cell-to-cell messaging and signal transduction[22]. Myoinositol is classified as a B vitamin, and is a common food additive, especially in cereals and foods rich in bran[22,23]. Reported concentrations of myoinositol detected in urine samples average 22.4 μM/mM creatine, with a maximum detected value of 36.1 μM/mM creatine[1]. Expelled concentrations of myoinositol in the urine are dependent on dietary intake, and may vary with a strict, preplanned flight mission diet. For use during space exploration, recovered myoinositol shows the most potential as a food additive or as a vitamin supplement.

*3. Aliphatic heteromonocyclic compounds*

Aliphatic heteromonocyclic compounds are a class of organic compounds containing a ring structure, either aromatic or nonaromatic, comprised of more than one kind of atom, usually carbon and another atom. Of the 43 compounds detected in urine that are within the aliphatic heteromonocyclic compounds superclass[1], only three were detected with 100% occurrence and a concentration average above 10 μM/mM creatine. The 10 μM/mM creatine average value qualification was determined in order to rule out trace elements that would be difficult to isolate in large enough concentrations to justify resource recovery.

Allantoin ($C_4H_6N_4O_3$) is a diureide of glyoxylic acid that is a primary product of the oxidation of uric acid[24,25]. Allantoin is present in the body through consumption and microbial production. High levels of allantoin in the urine

can be an indication of microbial overgrowth or oxidative stress[24]. Isolates of allantoin from comfrey plants are found in many cosmetic, hygiene and therapeutic substances. The addition of allantoin to sun care products and anti-acne treatments is used to assist with healing and to reduce irritation and swelling. Allantoin is also an ingredient in oral hygiene care products, such as toothpastes and mouthwash, and in pharmaceutical creams and treatments, such as shampoos and lotions. The average detected concentration of allantoin from urine is 15.4 μM/mM creatine, with a maximum detected value of 29.3 μM/mM creatine[1]. While increased production of allantoin in the body is not preferred[24], recovery could allow for the synthesis of a therapeutic agent used to reduce swelling and irritation, as skin irritation and other dermatological issues are one of the most common medical problems reported during spaceflight[26,27].

Creatinine ($C_4H_7N_3O$) is the product of dehydration reactions that break down creatine phosphate in the muscles[28,29]. The presence of creatinine in the urine is dependent on relative muscle mass, level of hydration, and the consumption of diuretics. Average concentrations of creatinine detected in urine are 14,743 μM/mM creatine, with a maximum concentration of 24,540 μM/mM creatine[1]. Typically, the production of a simple waste product, like creatinine, would not be of any value to resource recovery systems, unless it can be repurposed. By controlling the pH to produce a basic or neutral processing environment, isolated creatinine can be converted into creatine[28,29]. Using excreted creatinine wastes to reverse synthesize creatine can improve *in situ* food and supplement for spaceflight, as creatine is a common supplement for muscle function.

Pyroglutamic acid ($C_5H_7NO_3$) is the cyclized derivative of L-glutamic acid and glutamine, and while its derivative presence is relatively uncommon, it is detected in urine with 100% occurence[30]. Pyroglutamic acid is formed when the free amino group of glutamic acid cyclizes to form lactam, which is found in many proteins[31]. Cleavage of the pyroglutamate residue via pyroglutamate aminopeptidase restores the glutamic acid to its standard form[31]. Pyroglutamic acid has been detected in urine samples with an average concentration of 20.7 μM/mM creatine, and a maximum detected value of 32.6 μM/mM creatine[1]. Spaceflight applications for pyroglutamic acid are limited to therapeutic synthesis and food supplementation. Cleavage and conversion of isolated pyroglutamic acid to glutamic acid could be used in food supplement synthesis, yet glutamic acid is a non-essential amino acid, and may not be absorbed. Pyroglutamic acid has been named in many patents for therapeutics[31], specifically for bacterial infection[32] and Hepatitis C virus replication inhibition[33], and is sold as an over-the-counter therapeutic that claims to improve vascular function[30].

### B. Alkaloids and Alkaloid Derivatives

Alkaloids and alkaloid derivatives comprise a trace amount of the major components in urine, but are represented by trigonelline ($C_7H_7NO_2$)[1,34]. Trigonelline, a phytochemical alkaloid, is naturally produced in the seeds of many plant species, as well as sea urchin and jellyfish, specifically *A. pustullosa* and *V. spirans* respectively[35]. The presence of trigonelline in the body is dependent on dietary sources, specifically with consumption of oats, peas, hemp seeds, potatoes, coffee, and soybeans[34,35]. Sources of vitamin B3, or niacin, also contribute to secreted levels, as trigonelline is a direct product of niacin metabolism[35]. Concentrations of trigonelline detected in human urine average 31.1 μM/mM creatine, with a maximum concentration of 109.3 μM/mM creatine detected[1]. Trigonelline, most commonly isolated from fenugreek (*Trigonella foenumgraecum*), is a prominent staple in traditional Chinese medicine due to the hypoglycemic, hypolipidemic, neuroprotective, antimigraine, sedative, memory-improving, antibacterial, antiviral, and anti-tumorogenesis effects[36]. Studies have illustrated positive effects of trigonelline on diabetic complications and central nervous system diseases, as well as insulin secretion, glucose metabolism, neuron activation, β cell regeneration[36], and oxidative stress[37,38]. Recovery of trigonelline could be a potential candidate for therapeutic applications during spaceflight, but further research would be required to determine the long-term pharmacological toxicity and side effects.

### C. Amino Acids and Peptides

Amino acids and peptides are involved in many biological functions, such as protein synthesis and neurotransmitter synthesis and transport. Most amino acids, labeled non-essential, are synthesized *in vivo*, whereas some, termed essential amino acids, are required from dietary sources for continuation of proper biological function. The amino acids, peptides and analogues superclass is responsible for the highest number of compounds represented in urine with a 100% occurrence rate. Of the 286 compounds within the amino acids, peptides and analogues superclass, 17 compounds were identified with 100% occurrence and concentrations above 10 μM/mM creatine.

3-Aminoisobutanoic acid ($C_4H_9NO_2$) is the product of N-carbamyl-beta-aminoisobutyric acid conversion via the enzyme beta-ureidopropionase during the last step of pyrimidine degradation, which leads to activation of the citric acid cycle[39,40]. The presence of 3-aminoisobutanoic acid can act as an indicator for the metabolism of DNA and

RNA in both normal and tumorous tissues[41]. 3-Aminoisobutanoic acid is present in urine with a 100% occurrence rate, at an average concentration of 26.0 μM/mM creatine, with a maximum detected concentration of 140.0 μM/mM creatine[1]. Recovery of 3-aminoisobutanoic acid would have a limited range of applications for spaceflight. While there is some documentation for medicinal use for the delivery of anticancer drugs[42] and treatment of cataracts, macular degeneration and other ophthalmic diseases[43], publications detailing the use of 3-aminoisobutanoic acid are primarily focused on research application and manipulation of biosynthetic cycles.

3-Methylhistidine ($C_7H_{11}N_3O_2$) is an amino acid product of peptide bond synthesis and methylation of actin and myosin[44,45]. The presence of 3-methylhistidine in urine is an indicator of protein and fat metabolism, and of the rate of muscle breakdown[44,46,47]. The rates of muscle breakdown primarily depend on the health of an individual, and the regular stress on muscles, via exercise, illness and disease, or age. The average concentration of 3-methylhistidine in urine is 16.5 μM/mM creatine[1]. Maximum detected concentrations have been reported as 59.8 μM/mM creatine[1]. High levels of 3-methylhistidine in the urine indicate an active catabolism of muscle protein, which may be illustrative of malnutrition[47], poor antioxidant nutrition[48], or conditions associated with nitrogen loss[46]. Despite the numerous patents that have been filed naming it as a potential inhibitor of hepatitis C virus, the majority of the published research on the biomedical applications of 3-methylhistidine only identifies it as a sensitive indicator for muscle catabolism.

Creatine ($C_4H_9N_3O_2$) is a non-protein amino acid that acts as an energy shuttle and, upon conversion to phosphocreatine, acts an energy storage mechanism as well[49,50]. The phosphate group of adenosine triphosphate (ATP) is transferred to creatine, forming phosphocreatine, and then released with the synthesis of creatine kinase[49,50]. Creatine is synthesized by the liver from amino acids L-arginine, glycine and L-methionine, and stored in skeletal muscle and various organ tissues, such as the brain and heart[49]. Dietary intake can also supplement creatine synthesis in the body, as it is absorbed from the small intestines[50]. Creatine has been detected in human urine with an average concentration of 46.0 μM/mM creatine, and a maximum detected concentration of 448.0 μM/mM creatine[1]. The broad range of concentrations of creatine in urine can be attributed to dietary intake of creatine supplementation, activity level and athletic ability, age, gender[1], and overall health[49-53]. The most apparent application for creatine recovery from urine is as a food supplement. Previous studies have shown the general safety of taking creatine supplements to increase athletic ability, reduce recovery time between workouts, increase mental focus and reduce overall fatigue[51,52]. Supplements including recovered creatine may increase the physical and mental ability of crewmembers while reducing fatigue in microgravity environments. However, research is necessary to determine the side effects of creatine usage in microgravity environments, and the body's ability to utilize the supplement efficiently and effectively.

Glycine ($C_2H_5NO_2$) is a non-essential amino acid that is an integral part of DNA and phospholipid production, as well as energy release[54,55]. While deemed non-essential for dietary intake, glycine is found in many foods, such as gelatin and sugarcane, and is also a common food additive[55]. Glycine is used as a pharmacological agent as an irrigant for surgical techniques, an oral vasodilator, an inhibitory neurotransmitter, and as a preparatory agent for antacids[55,56]. Glycine is found in many personal care and hygiene products, such as facial cleanser, shampoo, conditioners, and deodorants[57]. The average concentration of glycine detected in human urine is reported as 106.0 μM/mM creatine, with a maximum of 300.0 μM/mM creatine[1]. The recovery of glycine from urine wastestreams during spaceflight has the potential to be used as a food additive[55], for the synthesis of creatine[49], as an ingredient for hygiene product synthesis, and may be useful for biomedical applications.

Guanidoacetic acid ($C_3H_7N_3O_2$) is a metabolite within the urea cycle, and acts as a precursor of creatine through the metabolic pathways of many amino acids, specifically glycine, serine, threonine, arginine, and proline[58,59]. Concentrations of guanidoacetic acid (GAA) detected in human urine samples average 41.8 μM/mM creatine[1]. Maximum GAA detection was detected in concentrations of 97.3 μM/mM creatine. Despite the widespread acceptance of creatine supplementation and dietary intake, the use of GAA as a food additive for restoring creatine availability via amino acid metabolic pathways has been restricted due to limited research concluding its safety and efficacy[60]. Research involving GAA oral supplementation has detailed positive effects in subjects with cardiac decompensation[61] and circulatory issues, arthritis[62], anxiety[63], and depression[60]. The spaceflight applications for recovered GAA from urine wastes may be beneficial to the development of therapeutics or supplementation for creatine metabolism. Even though prior reports identify a lack of side effects[60], further research will be required to determine potential side effects for usage of GAA supplementation and consumption in microgravity environments.

Hippuric acid ($C_9H_9NO_3$) is the primary form of glycine wastes that are removed from the body to reduce glycine accumulation in tissues and organs, such as the brain and cerebral spinal fluid, and the development of associated diseases[64,65]. Hippuric acid concentrations in human urine average 229.0 μM/mM creatine, with a maximum concentration of 622.0 μM/mM creatine detected[1,66]. The primary use of hippuric acid is as a biomarker for fruit and vegetable consumption in children[67], as well as glycine accumulation and the development of disease[65].

Recovered hippuric acid in pure form does not have any other obvious applications for spaceflight, due to its lack of diverse applications here on earth. Hippuric acid can be converted to urea[68], which, as stated previously, may have potential applications during spaceflight in synthetic fertilizers, as fuel supplementation, and as a building block molecule for product synthesis.

L-Alanine ($C_3H_7NO_2$) is an important amino acid that can act as an energy source when concentrated on muscle tissues[69], and regulates glucose metabolism[69,70]. Metabolism of L-alanine is dependent on the presence of vitamin B6, and can act as an inhibitory neurotransmitter[69,70]. Despite being a non-essential amino acid, L-alanine is regularly supplemented through dietary consumption of meat products and other high-protein foods[69]. Concentrations of L-alanine detected in human urine can average 21.8 μM/mM creatine[1]. Concentrations of L-alanine can fluctuate depending on dietary intake and the rates of metabolism. The most applicable potential for spaceflight application is to use L-alanine as a therapeutic. L-alanine can be used to reduce severe hypoglycemia and ketosis associated with diabetes[69,70], and to increase lymphocyte reproduction *in vitro*[69,71]. The effects of L-alanine on immune system function and glucose metabolism may be of use for therapeutics during long duration missions, but would require extensive research to determine the validity of these effects.

L-Aspartic acid ($C_4H_7NO_4$), also known as aspartate, is a proteinogenic amino acid, which plays important roles in the urea cycle and DNA metabolism[72,73]. L-Aspartic acid is found in urine with an average concentration of 10.9 μM/mM creatine, with a maximum reported concentration of 21.8 μM/mM creatine[1]. L-aspartic acid acts as an excitatory neurotransmitter, and can raise blood levels when supplemented in 5 grams or more[72]. Dietary intake is common, as L-aspartic acid combined with phenylalanine comprises aspartame, a natural sweetener[72,73]. Given the approval as a food additive, consumption and supplementation in regulated dosages is assumed to be safe. While the most likely use of recovered L-aspartic acid during spaceflight would be as a food additive and sweetener, studies have shown L-aspartic acid, specifically in the form of zinc aspartate, to protect against radiation exposure and the associated damaging effects[74,75]. Further research is required to determine the best-suited application for recovered L-aspartic acid in spaceflight environments.

L-Cysteine ($C_3H_7NO_2S$) is a thiol-containing amino acid that is found in most proteins[76]. The inclusion of a thiol group allows L-cysteine to undergo reduction/oxidation reactions, or redox reactions. When oxidized, or when electrons are lost, L-cysteine forms cystine via the formation of a disulfide bond. The addition of electrons, or reduction, reverses oxidation, producing two L-cysteine molecules from one L-cystine molecule. L-Cysteine has been reported in human urine with an average concentration of 65.8 μM/mM creatine, with 134.5 μM/mM creatine as the maximum reported concentration detected[1]. L-Cysteine has antioxidant properties[78] and is important for energy metabolism[76,77]. Clinically, L-cysteine is used as a therapeutic for psoriasis and other skin ailments, as an accelerant for regeneration of the ocular epithelium[77,78], and as a treatment for asthmatics[78]. Based on the normality of current therapeutic uses of L-cysteine, recovered L-cysteine from urine during spaceflight would most likely be used for medical treatment and therapeutic synthesis.

L-Cystine ($C_6H_{12}N_2O_4S_2$) is an amino acid that is formed by the oxidation and dimerization of L-cysteine[76] and is present in human urine with average concentration of 12.5 μM/mM creatine[1]. L-Cystine is a structural component of many tissues and hormones[76,79,80], and plays important roles in protein digestion, folding and absorption, cysteine metabolism, and transportation of substrates, such as lipids, sugars, ions, peptides, sterols, and proteins[80]. While L-cystine is not currently used as a pharmacological or therapeutic agent, the conversion of L-cystine to L-cysteine involves a simple reduction. The best application in spaceflight for recovered L-cystine is to supplement the L-cysteine stocks for therapeutic synthesis.

L-Glutamine ($C_5H_{10}N_2O_3$) is an abundant, free amino acid[81] that is found in high-protein foods, such as fish, red meat, dairy and beans[82,83], and is a common supplement for athletes and bodybuilders[82]. L-Glutamine contributes to the production of other amino acids, nucleotides, proteins, and glucose, and acts as a metabolic energy source for many cell types, including enterocytes, lymphocytes, macrophages, and fibroblasts[84]. L-Glutamine also acts as a nitrogen shuttle, converting excess ammonia into urea[84]. Dietary supplementation of L-glutamine has been shown to reduce muscle cramps, reduce recovery time between workouts, and maintain barrier functions within the digestive tract[83] without reports of negative side effects[82]. Concentrations of L-glutamine reported in human urine average 37.2 μM/mM creatine, with a maximum detected concentration of 77.9 μM/mM creatine[1]. The bioavailability of L-glutamine is positive for resource recovery, as therapeutic use is widely accepted for a number of applications[82-84]. Prescription of L-glutamine is common for patients that have undergone abdominal surgeries, as it can prevent bacterial translocation, which reduces the risk of sepsis and multiple organ failure[84]. Research has also shown the involvement of L-glutamine with tumor growth and suppression, which opens opportunities for the development of cancer-related therapeutics[81,83-85]. As a result of the broad acceptance of L-glutamine use as a dietary supplement and therapeutic agent, recovery of L-glutamine from urine wastes could fulfill food supplement and therapeutic development for long duration space applications.

L-Histidine ($C_6H_9N_3O_2$) is an essential amino acid that is a precursor for histamine and carnosine biosynthesis[86,87]. Concentrations of L-histidine reported in human urine average 43.0 μM/mM creatine, with a maximum detected concentration of 90.0 μM/mM creatine[1,86]. L-Histidine harnesses antioxidant, anti-inflammatory, and anti-secretory properties by inhibiting cytokines and growth factors that induce cell and tissue damage during, and as a result of an immune response[86,88,89]. The most common uses for L-histidine are medicines and therapeutics, food additives and dietary supplements, and for biomedical research and assays[90]. Depending on the concentrations of L-histidine in the foods available to crewmembers, recovered concentrations of L-histidine from urine wastes may be recycled as dietary supplements to assist in meeting the daily required intake values of the essential amino acid. Based on the current uses of L-histamine for earth-based applications, regular consumption of recovered L-histidine may reduce incidence rates of inflammation and improve histamine production in crewmembers.

L-Lysine ($C_6H_{14}N_2O_2$) is an essential amino acid[91,92] that occurs in human urine with an average concentration of 17.2 μM/mM creatine, and a maximum report of 51.3 μM/mM creatine[1,91]. Dietary intake of L-lysine is dependent on consumption of lean protein foods, including poultry, cottage cheese, and pork[91]. Concentrations of L-lysine are minimal in fruit and vegetable sources, except for avocados and wheat germ[91]. The high concentration of L-lysine in meats and animal byproduct foods may be due to the fact that L-lysine is a common supplement added to animal feed[92]. L-Lysine is involved in many biological processes, such as receptor affinity, protease cleavage, retention of endoplasmic reticulum, nuclear structure and function, muscle elasticity, and chelation of heavy metals[92]. Adequate consumption of L-lysine may be useful in the treatment of and protection against osteoporosis[91] by increasing calcium absportion[93]. Research has shown that L-lysine may be a key component in the solubility and uptake of many pharmaceuticals that may otherwise be unable to pass through cell membranes and tissues[92,94,95]. While L-lysine isn't typically used as a dietary supplement, and consumption is dependent on lysine-rich foods, recovered L-lysine could potentially be utilized to improve absorption or synthesize new therapeutics for use during long duration missions.

L-Serine ($C_3H_7NO_3$) is a non-essential amino acid that contributes to protein synthesis and tissue development[96,97]. L-Serine is synthesized *in vivo* through protein and phospholipid degradation and via the glycolytic intermediate 3-phosphoglycerate[96], but can also be made available through dietary intake of meats, soy, and seaweed[98]. L-Serine is present in human urine with an average concentration of 25.3 μM/mM creatine[1]. The non-essential classification of L-serine has been challenged by research illustrating the predominant role it plays with cell culture, tissue development, and central nervous system functioning[99]. Some studies report the specific importance of L-serine with brain development and functioning, and that regular consumption of L-serine supplements may be a viable treatment for chronic fatigue syndrome[97,99]. Crewmembers may require supplementation from vitamins and food additives during long duration missions, as serine-rich foods, especially meats, which may not be included in the diet plans.

L-Threonine ($C_4H_9NO_3$) is an essential amino acid that is required for neurological functioning and thymus development and functioning through immunostimulation[100,101]. Presence of L-threonine in urine is dependent on efficient threonine catabolism and dietary intake of L-threonine-rich foods, such as meats, cottage cheese and wheat germ[100]. On average, L-threonine concentrations in urine average 13.3 μM/mM creatine[1] in normal, healthy adults. The consumption of L-threonine is required for standard bio-utilization, but inadequate catabolism, overconsumption with dietary intake, or inadequate removal as a bio-waste, can lead to high levels of accumulation that can concentrate in the brain and affect neurotransmitter balance[100,101,102]. L-Threonine recovery from urine sources could have a potential as a food supplement for long duration missions.

Phenylacetylglutamine ($C_{13}H_{16}N_2O_4$) is an amino acid acetylation product of phenylacetate[103,104], and is an important regulator of the urea cycle[105,106], which converts ammonia into urea for disposal. On average, phenylacetylglutamine is present in urine in concentrations of 34.0 μM/mM creatine, with a maximum reported detected concentration of 70.0 μM/mM creatine[1]. Other than its use in clinical research as a biomarker for urea cycle disorders[105,106], there are not many applications for the nitrogenous waste product phenylacetylglutamine. Recovery of phenylacetyglutamine from urine during spaceflight could potentially be utilized for its nitrogen molecules.

### D. Carbohydrates

The carbohydrates superclass is comprised of many compounds that are essential for central metabolism. Carbohydrates are generally distributed between four chemical groups: monosaccharides, disaccharides, oligosaccharides, and polysaccharides[107]. Monosaccharides are the simplest, primary form of carbohydrates, in that they cannot be hydrolyzed into smaller carbohydrate molecules, and are the building blocks that comprise polysaccharides[107,108]. Monosaccharides are a critical fuel source in the body, and are also fundamental components of nucleic acids[107-109]. Polysaccharides, which are the secondary (disaccharides), tertiary (oligosaccharides), and quaternary forms of carbohydrates, are multiple monosaccharides linked together for the synthesis of a more

complex and often energy efficient sugar[107]. Polysaccharides are involved in energy storage[107,108], cell-to-cell recognition[107], DNA synthesis[109], and the development and maintenance of biomembranes and structures[107]. Of the 116 compounds identified from urine samples within the carbohydrates and carbohydrate conjugates superclass[1], only 14 were detectable with a minimum of 10.0 μM/mM creatine and a 100% occurrence rate.

Arabinitol ($C_5H_{12}O_5$), also known as arabitol, is a five-carbon sugar alcohol[110,111] that is present in urine samples with an average concentration of 31.8 μM/mM creatine[1]. Biosynthesis of arabinitol is achieved through reduction of the carbonyl group of xylose[111]. While some amount of arabinitol in the urine is expected, increased levels may indicate yeast infection[112], transaldolase deficiency, and cirrhosis of the liver[110]. There are limited uses for arabinitol, as it is generally produced as a biochemical byproduct in the body. Given the sucrose-mimicking sweetness of arabinitol, the most common usage is as a non-cariogenic sweetener[111,113]. Recovery of arabinitol from urine wastes may enhance the ability to synthesize palatable food products in space. Research will be required to determine the long-term health effects with consuming arabinitol-containing foods regularly.

D-Galactose ($C_6H_{12}O_6$) is an energy-providing aldohexose that occurs naturally in lactose, cerebrosides, gangliosides, and mucoproteins, and is important for the biosynthesis of many macromolecules[114,115]. D-galactose is found in urine at an average concentration of 11.9 μM/mM creatine, and a maximum reported concentration of 25.2 μM/mM creatine[1]. D-galactose is naturally found in milk and a number of fruits and vegetables[115], and is most commonly found as a food additive in the form of carrageenan[115,116], which acts as an emulsifier and thickening or gelling agent[116], as an alternative for gelatin. The thickening properties of D-galactose in the form of carrageenan are due to its high negative charge, and are also used in cosmetic lotions and creams[116]. Recovered D-galactose could potentially be utilized to produce food supplements and products in various forms during spaceflight. The thickening and gelling properties of D-galactose may be altered in space environments, and further research will be required before use.

D-Glucose ($C_6H_{12}O_6$) is the primary energy source for living organisms, and is available for dietary intake from fruits and plant foods[117,118]. D-Glucose is synthesized in the liver and kidneys via gluconeogenesis[117,118]. Concentrations of D-glucose detected in urine samples average 37.5 μM/mM creatine, with a maximum reported concentration of 58.4 μM/mM creatine[1]. Current uses for D-glucose include therapeutic injections for fluid and caloric replenishment, and as a sweetening agent in foods[118]. Recovery of D-glucose from urine wastes could potentially be applied to food products, or used for emergency medicine applications. D-glucose could be purified and used to make synthesized food products more enjoyable to consume, or used as a replenishing therapeutic for malnourished crewmembers.

D-Threitol ($C_4H_{10}O_4$), or erythritol, is a polyol[119], or an alcohol that contains multiple hydroxyl groups, that acts as the main end product of D-xylose metabolism[119,120]. Expelled concentrations of D-threitol are primarily found in urine, and may fluctuate with threitol consumption[120] or age[119]. Average concentrations of D-threitol in urine are reported as 19.3 μM/mM creatine[1]. Dietary intake of D-threitol is dependent on the consumption of foods that naturally contain D-threitol, such as fruits, vegetables, and fermented products, or foods with D-threitol added as a non-nutritive sweetener[120]. D-Threitol can also be used as an ingredient in firefighting materials, such as dry chemical sprays and foams[120]. To limit dangerous workloads for crewmembers, most firefighting materials are designed and assembled on earth, so the best application for recovered D-threitol during spaceflight would be as a non-nutritive sweetener and food additive.

D-Xylose ($C_5H_{10}O_5$) is a monosacharride that is essential for human to consume[121,122], due to its interaction with xylosyltransferase[123]. D-Xylose is a plant-based sugar, primarily found in the woods, barks, straws and hulls, as well as in plant embryos[122]. Concentrations of D-xylose in urine are reported as an average of 30.0 μM/mM creatine, with a maximum reported concentration of 102.0 μM/mM creatine[1]. D-Xylose can be used as a sweetener, although it is not as sweet as sucrose[122]. Interest in D-xylose has peaked in synthetic biology research communities, as some yeasts are able to convert D-xylose into ethanol[124,125]. NASA's interest in synthetic biology for the production of fuels for long duration missions has increased with the prospects of deep space and long duration planetary missions. Based on the positive results from converting D-xylose-containing biomass into biofuels on earth, recovery of D-xylose from urine wastes may be suited for applications with the synthesis of fuels and other chemicals.

Erythritol ($C_4H_{10}O_4$) is a sugar that is naturally sourced from algae, lichens and fungi that is twice as sweet as sucrose[106,107]. Erythritol can be produced by fermentation, making it a common ingredient in beer, wine, sake, and soy sauce[106]. As a small molecule, erythritol is able to easily pass through membranes easily without assistance or active transport[106]. Urine detection is based on consumption of erythritol-containing foods, such as algae, fungi, and sugar-free candies and supplements[107], as most of what is consumed is passed as a waste. Normal concentrations in human urine have a reported average of 33.4 μM/mM creatine[1]. An obvious application for recovered erythritol is as a food additive, yet it is also used as a coronary vasodilator[107]. Recovered concentrations of erythritol may be used

to create a more palatable food product that is synthesized during space flight, or added to existing food sources for sweetness, and may have therapeutic applications as a vasodilator.

Gluconic acid ($C_6H_{12}O_7$) is a naturally occurring carbohydrate that is primarily found in honey and fruits, and can be used as a food additive and acidity regulator[128]. Gluconic acid is found in urine samples in average concentrations of 21.5 μM/mM creatine, and has been reported as high as 38.8 μM/mM creatine[1]. Chemically, gluconic acid is a strong chelating agent, and is an ingredient in many "eco-friendly" cleaning products for its ability to break up mineral deposits[129,130]. Space applications for gluconic acid will most likely concentrate on the industrial benefits of gluconic acid, yet a stable acidity regulator may be required with the synthesis of food products.

Glycerol ($C_3H_8O_3$) is a trihydroxy sugar alcohol that is a primary component of triglycerides and phospholipids[131], and an intermediate for carbohydrate and lipid metabolism[132]. Glycerols are released into the urine when fat stores are metabolized as an energy source[131]. Glycerol is found in urine in average concentrations of 13.0 μM/mM creatine[1], and is dependent on consumption of glycerol-containing foods and the usage of stored fats. Usage of glycerol extends into many genres, including pharmaceutical, industrial, food additives, and home products[132,133]. Chemically, glycerol is a mild solvent, emollient[133], and cryoprotectant[132]. Recovery of glycerol from urine during spaceflight could be utilized as a building block molecule for the synthesis of a wide range of products, due to the broad applications it serves on earth.

Lactose ($C_{12}H_{22}O_{11}$) is the primary sugar in milk products, including human milks[134,135]. Humans produce lactase, a digestive enzyme, to metabolize milk sugars for a source of energy. After infancy, the main source of lactose is through dietary intake of other mammalian milks, primarily bovine, and with lactose-added foods. Lactose is often added as a sweetener to a variety of different types of processed foods[135]. Lactose is found in urine with average concentrations of 11.8 μM/mM creatine, with reported concentrations as high as 24.2 μM/mM creatine[1]. In addition to dietary sources, lactose is an ingredient in cosmetic and household items, such as creams and soaps[136]. Secretion of lactose may fluctuate depending on crewmembers' dietary exposure, and may not be a valuable compound for resource recovery for space applications. Further research is required, and will be most likely depend heavily on foods approved for long duration missions. If concentrations of lactose in crewmember urine are recoverable and deemed useful for recycling, lactose may be used for pharmaceutical delivery or the synthesis of food products and hygienic materials.

### E. Lipids

Lipids are plentiful and perform many essential functions within biological processes, such as creating hydropolarized barriers with the formation of lipid bilayers, or assisting in the trafficking of vitamins and minerals that are not easily absorbed by standard metabolic processes.

The most prominent lipid compound detected in urine is mannitol ($C_6H_{14}O_6$)[1]. Chemically, mannitol can also be classified as an alcohol and a sugar, or as a polyol[137,138]. When mannitol is found in aqueous solutions, it performs oxidation reactions to shed electrons, causing the solvent to become acidic[137,138]. On average, mannitol can be detected in urine in concentrations of 32.4 μM/mM creatine[1]. Humans poorly absorb mannitol. An increased presence in urine, in concentrations up to 85.1 μM/mM creatine[1], can be explained by the consumption of apples, pineapples, asparagus and carrots[1]. Mannitol is unable to cross biological membranes and has little energy value, but can act as a weak vasodilator and osmotic diuretic agent[137,138], allowing for pharmaceutical applications. Mannitol is also used as a food additive and sweetener, specifically in low calorie food products, which may be useful for food synthesis in space environments.

### F. Organic Acids

Organic acids comprise a large class of compounds found in urine, third only to amino acids and peptides, and carbohydrates.

Acetic acid ($C_2H_4O_2$) is a simple carboxylic acid that is produced by the oxidation of ethanol and the metabolic processes of bacteria, specifically *Acetobacter* genus and *Clostridium acetobutylicum*[139-141]. Acetic acid is essential to the metabolism of carbohydrates and fats, and can alter the pH levels within cells and organs in the body. Normal concentrations of acetic acid detected in the urine average 13.0 μM/mM creatine, and have been reported as high as 106.0 μM/mM creatine[1]. Excretion of acetic acid in the urine can be related to lung and GI tract absorption efficiencies from dietary intake, or exposure to acetic acid in pharmacological and industrial applications. For example, acetic acid is a common ingredient in the production of starches, sugars, wines, and vinegars[140-142]. Bacteria that produce acetic acid are found in environments common to food harvesting and production, in water, soil and within produce[139], making acetic acid a universally available compound. Acetic acid is also used industrially for the manufacturing of chemicals, explosives, lacquers, sealants, and household reagents and cleaning products[140-142]. The chemical applications of acetic acid compliment the intended emphasis on *in situ* synthesis of products for

long duration missions. Recovery of acetic acid from urine wastes may give rise to a compendium of applications in structural and life support areas of spaceflight.

Citric acid ($C_6H_8O_7$) is a weak acid that is formed in the tricarboxylic acid cycle[143], and acts as a primary intermediate in metabolic processes[144]. Citric acid can be synthesized in the body, or made available via dietary intake[143,144]. Concentrations of citric acid found in plasma and urine are often used as a diagnostic indicator for many diseases or metabolic difficulties[143,144]. In urine from healthy adults, citric acid is detected with an average concentration of 203.0 μM/mM creatine, and has been detected as high as 600.0 μM/mM creatine[1]. An increase in citric acid concentrations in urine is generally due to a heightened intake of fruits, specifically citrus varieties[143]. Citric acid is used as a food preservative and additive for tart and acidic flavor, most commonly found in beverages, soft drinks, candies, and confections[144]. Pharmaceutically, the salts of citric acid can be used as anticoagulants, as they have an affinity for chelating calcium[144,145]. In addition, citric acid is a main ingredient in many cleaning agents[146], and has become increasingly popular with the advent of "green", natural, and environmentally friendly cleaners. The recovery of citric acid from urine could provide a number of benefits to spaceflight technologies, including the synthesis of food products, chemical reagents, and life support products.

Formic acid ($CH_2O_2$), also known as formate, is the simplest form of carboxylic acid, and is an intermediate for normal metabolic processing, transmethylation[147], and chemical synthesis[148]. Formic acid is present in urine in average concentrations of 26.8 μM/mM creatine, and has been detected as high as 120.9 μM/mM creatine in standard samples[1]. The most recognizable source of formic acid in nature is in the venom associated with bee and ant stings[147,148]. Formic acid has shown strong antimicrobial properties, and can be used as a preservative that reduces the rates of degradation in biomass, such as straw and hay for livestock feed sources[148]. Formic acid is also used in household cleaners and chemical products, such as laundry detergents and fabric softeners[149]. For space applications, formic acid has the potential to be used for the preservation of food materials or as an antimicrobial agent.

Glycolic acid ($C_2H_4O_3$) is a small alpha-hydroxy acid (AHA) produced by oxidation of fatty acids and has the unique ability to easily penetrate the skin[150,151]. Due to its capability to penetrate thick epithelial layers, glycolic acid is often used for penetrative treatments for skin diseases, such as fungal infections and warts[151]. The penetrating properties of glycolic acid have made it a popular ingredient for household cleaners and automotive care products[152]. Average concentrations of glycolic acid in urine samples from healthy adults were reported as 42.0 μM/mM creatine, and were detected as high as 122.0 μM/mM creatine in some samples[1]. Glycolic acid could be used as a transport mechanism for therapeutic tissue penetration and topical applications for any therapeutics synthesized inflight, and may be used for its antifungal and antimicrobial properties. Chemically, glycolic acid has the potential to be used for the production and processing of textiles, metals, and adhesives, and for pH control in chemical synthesis[151]. The potential chemical applications for glycolic acid recovery from urine sources are broad, and will need to be assessed to determine the best fit for use during long duration missions.

L-Lactic acid ($C_3H_6O_3$) is an acid intermediate in the fermentation, or metabolism, of sugar and is produced during intensive muscle activity[153,154]. L-Lactic acid is found in normal urine samples in an average concentration of 11.6 μM/mM creatine[1], and can fluctuate based on the body's ability to clear it after production[153]. The uses for L-lactic acid are broad, and include applications in chemical synthesis and industrial material processing, as well as food additive applications, including cheese manufacturing, and candy production[155]. Like many of the compounds that can be recovered from urine, L-lactic acid has the potential to be utilized as a food additive during the synthesis of food products and supplements, and for its chemical and industrial applications. Research is required to determine the risk associated with using L-lactic acid as a food additive in space environments, and crewmember ability to clear consumed concentrations while avoiding toxicity associated with L-lactic acid accumulation. Consumption of L-lactic acid as a food additive is safe on Earth, but the standard physiological changes seen in microgravity may need to be investigated further to avoid the onset of lactic acidosis[156,157].

Taurine ($C_2H_7NO_3S$) is a sulfur-containing amino acid that is essential for mammalian development[158,159], and can be detected in urine at an average concentration of 81.0 μM/mM creatine, with a maximum reported value of 251.0 μM/mM creatine[1]. Concentrations of taurine can be found in the brain, heart, breast tissue, gall bladder and kidneys, and serves as a neurotransmitter, a stabilizer of cell membranes, and a facilitator for the transport of ions[158]. While taurine can be synthesized in the body, it is dependent on the presence of vitamin B6[158,159]. Taurine has become a popular additive in energy drinks[159], which depend on taurine's ability to improve athletic performance[158,159], and cardiovascular performance[160]. Even though taurine is produced internally, some researchers believe some consumption of taurine from dietary intake is essential for maintaining proper physiological function, and to avoid diseases, such as depression, and other neurological disorders[158] that may be associated with decreased levels of taurine in the body. Given the importance of taurine on major organ function and physical ability, recovered taurine should be considered as a potential therapeutic supplement for crewmembers.

## G. Potential Applications and Challenges

The following chart (Table 2) summarizes the extensive overview of each superclass and the compounds that illustrate the most potential for resource recovery and downstream applications during long duration missions.

**Table 2: Summarization of Identified Compounds, Including Average Concentrations and Potential Applications for Space**

| Superclass | Compound | Molecular Formula | Average Concentration in Urine | Potential Space Applications |
|---|---|---|---|---|
| Aliphatic Compounds | Dimethylamine | $C_2H_7N$ | 30.8 µM/mM creatine | Chemical |
| | Ethanolamine | $C_2H_7NO$ | 33.4 µM/mM creatine | Chemical |
| | Methanol | $CH_4O$ | 37.0 µM/mM creatine | Chemical |
| | Trimethylamine N-oxide | $C_3H_9NO$ | 91.0 µM/mM creatine | Therapeutic |
| | Urea | $CH_4N_2O$ | 12,285.0 µM/mM creatine | Chemical |
| | Myoinositol | $C_6H_{12}O_6$ | 22.4 µM/mM creatine | Food |
| | Allantoin | $C_4H_6N_4O_3$ | 15.4 µM/mM creatine | Therapeutic |
| | Creatinine | $C_4H_7N_3O$ | 14,743.0 µM/mM creatine | Food |
| | Pyroglutamic acid | $C_5H_7NO_3$ | 20.7 µM/mM creatine | Food, Therapeutic |
| Alkaloids & Alkaloid Derivatives | Trigonelline | $C_7H_7NO_2$ | 31.1 µM/mM creatine | Therapeutic |
| Amino Acids & Peptides | 3-Aminoisobutanoic acid | $C_4H_9NO_2$ | 26.0 µM/mM creatine | Chemical |
| | 3-Methylhistidine | $C_7H_{11}N_3O_2$ | 16.5 µM/mM creatine | Therapeutic |
| | Creatine | $C_4H_9N_3O_2$ | 46.0 µM/mM creatine | Food |
| | Glycine | $C_2H_5NO_2$ | 106.0 µM/mM creatine | Food |
| | Guanidoacetic acid | $C_3H_7N_3O_2$ | 41.8 µM/mM creatine | Therapeutic |
| | Hippuric acid | $C_9H_9NO_3$ | 229.0 µM/mM creatine | Chemical |
| | L-Alanine | $C_3H_7NO_2$ | 21.8 µM/mM creatine | Therapeutic |
| | L-Aspartic acid | $C_4H_7NO_4$ | 10.9 µM/mM creatine | Food |
| | L-Cysteine | $C_4H_7NO_4$ | 65.8 µM/mM creatine | Therapeutic |
| | L-Cystine | $C_6H_{12}N_2O_4S_2$ | 12.5 µM/mM creatine | Therapeutic |
| | L-Glutamine | $C_5H_{10}N_2O_3$ | 37.2 µM/mM creatine | Food, Therapeutic |
| | L-Histidine | $C_6H_9N_3O_2$ | 43.0 µM/mM creatine | Food |
| | L-Lysine | $C_6H_{14}N_2O_2$ | 17.2 µM/mM creatine | Therapeutic |
| | L-Serine | $C_3H_7NO_3$ | 25.3 µM/mM creatine | Food |
| | L-Threonine | $C_4H_9NO_3$ | 13.3 µM/mM creatine | Food |
| | Phenylacetylglutamine | $C_{13}H_{16}N_2O_4$ | 34.0 µM/mM creatine | Chemical |
| Carbohydrates | Arabinitol | $C_5H_{12}O_5$ | 31.8 µM/mM creatine | Food |
| | D-Galactose | $C_6H_{12}O_6$ | 11.9 µM/mM creatine | Food |
| | D-Glucose | $C_6H_{12}O_6$ | 37.5 µM/mM creatine | Food, Therapeutic |
| | D-Threitol | $C_4H_{10}O_4$ | 19.3 µM/mM creatine | Food |
| | D-Xylose | $C_5H_{10}O_5$ | 30.0 µM/mM creatine | Chemical |
| | Erythritol | $C_4H_{10}O_4$ | 33.4 µM/mM creatine | Food |
| | Gluconic acid | $C_6H_{12}O_7$ | 21.5 µM/mM creatine | Chemical |
| | Glycerol | $C_3H_8O_3$ | 13.0 µM/mM creatine | Food, Chemical, Therapeutic |
| | Lactose | $C_{12}H_{22}O_{11}$ | 11.8 µM/mM creatine | Food, Chemical |
| Lipids | Mannitol | $C_6H_{14}O_6$ | 32.4 µM/mM creatine | Food, Therapeutic |
| Organic Acids | Acetic acid | $C_2H_4O_2$ | 13.0 µM/mM creatine | Chemical |
| | Citric acid | $C_6H_8O_7$ | 203.0 µM/mM creatine | Food, Chemical |
| | Formic acid | $CH_2O_2$ | 26.8 µM/mM creatine | Food, Therapeutic |
| | Glycolic acid | $C_2H_4O_3$ | 42.0 µM/mM creatine | Chemical |
| | L-Lactic acid | $C_3H_6O_3$ | 116.0 µM/mM creatine | Food, Chemical |
| | Taurine | $C_2H_7NO_3S$ | 81.0 µM/mM creatine | Therapeutic |

The diversity of the identified compounds could allow for a broad range of needs and requirements to be met without ground-based support, but will be dependent on the ability to overcome the challenges associated with recovering resources from concentrated wastes. The most prevalent challenge will be the instability of urine after it

is voided. Some compounds may react with the external environment or be degraded by bacteria to create undesired compounds. Additionally, the pH of urine can change with the degradation of compounds, which may not be suitable for secondary processing.

Secondary treatment will be required for purification, and may add mass and cost for a minimal recovery payoff. Economic and cost-benefit analyses will need to be performed in order to determine if an operation involving resource recovery of this magnitude is feasible for long duration missions. Technologies currently used for the recovery of water utilize membranes in physico-chemical filtration processes.

Primary technologies utilized for the recovery of solutes and solvents include pressurized systems and membrane filtration. Membranes and columns utilized for resource recovery from urine streams will require heightened selectivity, to reduce the potential for contamination, and the ability to withstand exposure to concentrated wastes with minimal maintenance or replacement. Longevity of membranes and other technologies will affect the final recovered product, and may require fail-safe measures to reduce the transference of unwanted contaminants and constituents.

An alternative concept for the reuse of compounds and metabolites from urine is to retain the compounds with nutritious value in solution with the recovered water. Instead of focusing technology development towards removing small molar concentrations of valuable compounds, intending to remove the true wastes, such as the inorganic salts, urea, ammoniums and other nitrogenous compounds, may be a more achievable goal. Additionally, removing compounds without further neutraceutical benefits may lead to the synthesis of a nutritious drink supplement comprised of water and beneficial compounds from urine wastes. Secondary treatment of such a product would be required to ensure proper filtration and removal of potential contaminants, whether biological or chemical.

## III. Conclusion

The need for material recycling and resource recovery will be emphasized with increases to mission duration and distance traveled. The number of compounds available for recovery from urine wastestreams is extensive[1], but will only begin to address the required resources for long duration missions.

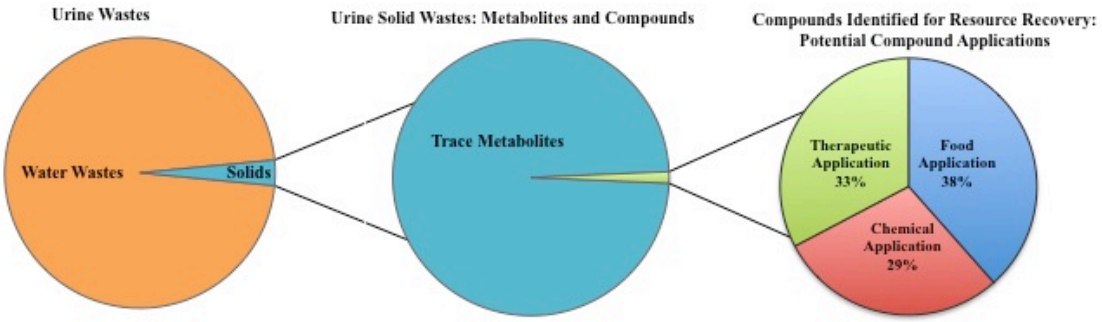


**Figure 1: Exploded Pie Charts Representing the Concentration of Urine Compounds Identified for Potential Resource Recovery in Space.** *Expanding the values of urine waste components from Table 1, urine is comprised mostly of water. The amount of solid components of urine may seem minimal when compared to the fluid component of wastes, but is comprised of a large number of solutes. Bouatra, et al. (2013) identified over 3,000 metabolites and compounds within urine, expanding the diversity of the solid waste components of urine. The small group of compounds discussed in this paper was selected from the compendium of compounds described by Bouatra, et al. (2013). Of the compounds identified for potential use during spaceflight, 38% showed promise for food applications, 33% for therapeutic applications, and the remaining 29% for chemical applications.*

A majority of the compounds discussed in this review show clear applicability to either food applications, therapeutic applications, or chemical applications (Figure 1). Compounds with food applications could serve as food additives to enhance preservation or to assist in the synthesis of food products, or as supplements to ensure the availability of a well rounded diet and essential nutrient intake for crewmembers. Compounds with the potential for therapeutic applications could aid in the synthesis of pharmaceutical products, or be used for a direct medical application. Many of the compounds with therapeutic applications are able to elicit a physiological response, such as vasodilation or moderation of the immune response, through calculated dietary intake. Compounds with the

potential for chemical application could be used as building block molecules for the synthesis of structural, life support or fuel products. Additionally, some compounds could be useful in their purified form for research that may be performed onboard. The compounds identified in this review showed a relatively even distribution between potential avenues for application, which highlights the relevancy of urine for resource recovery. Future research could be useful in identifying the necessary technologies required for the recovery and reuse of target compounds.

The success of long-duration missions will depend on the development of technologies that recover valuable resources from unavoidable wastes. The current technologies utilized on the ISS for water recovery from urine wastes discard brines and solids, instead of recovering the beneficial constituents. Utilizing all the available nutrients and compounds will increase the self-sustainability of long duration missions, which may allow for a greater level of independence from ground-based support. Given the broad chemical composition of urine, the downstream benefits of urine processing for resource recovery will be critical for many aspects of crewmember support, such as life support processes, food production, and the synthesis of fuels.

## References


[1]Bouatra, S., *et. Al*, "The Human Urine Metabolome," *PLOS One*, Vol. 8, No. 9, 2013.

[2]Hanford, A. J., "Advanced Life Support Baseline Values and Assumptions Document," *National Aeronautics and Space Administration*, NASA CR-2004-208941, 2004, pp. 27, 105.

[3]Putnam, D. F., "Composition and Concentrative Properties of Human Urine," *National Aeronautics and Space Administration*, NASA CR-1802, 1997

[4]Echeverry, G., Hortin, G. L., and R, A. J., "Introduction to Urinalysis: Historical Perspectives and Clinical Application," *Methods in Molecular Biology*, Vol. 641, Ch. 1, 2010.

[5]Zeeman, G. and Kujawa-Roeleveld, K., "Resource recovery from source separated domestic waste(water) streams; full scale results," *Water Science & Technology*, Vol. 64, No. 10, 2011.

[6]Kirchmann, H., and Pettersson, S., "Human urine – Chemical composition and fertilizer use efficiency," *Fertilizer Research*, Vol. 40, 1995, pp. 149-154.

[7]Occupational Safety and Health Administration "Dimethylamine," *Sampling and Analytical Methods*, URL: https://www.osha.gov/dts/sltc/methods/organic/org034/org034.html, [cited 11 Feb 2014].

[8]The Metabolomics Innovation Center (TMIC), "Dimethylamine (HMDB00087) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: www.hmdb.ca/metabolites/HMDB00087, [cited 10 Feb 2014].

[9]National Center for Biotechnology Information (NCBI), "Dimethylamine (CID 674)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=674, [cited 10 Feb 2014] .

[10]The Metabolomics Innovation Center (TMIC), "Ethanolamine (HMDB00149) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00149, [cited 10 Feb 2014].

[11]Moody, J. D., Heinze, T. M., Hansen, E. B. Jr., Cerniglia, C. E., "Metabolism of the ethanolamine-type antihistamine diphenhydramine (Benadryl) by the fungus Cunninghamella elegans," *Applied Microbiology and Biotechnology*, Vol. 53, No. 3, 2000, pp. 310-315.

[12]National Center for Biotechnology Information (NCBI), "Ethanolamine (CID 700)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=700 [cited 10 Feb 2014] .

[13]The Metabolomics Innovation Center (TMIC), "Methanol (HMDB01875) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb01875, [cited 10 Feb 2014].

[14]National Center for Biotechnology Information (NCBI), "Methanol (CID 887)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=887 [cited 10 Feb 2014] .

[15]The Metabolomics Innovation Center (TMIC), "Trimethylamine N-oxide (HMDB00925) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00925, [cited 10 Feb 2014].

[16]National Center for Biotechnology Information (NCBI), "Trimethylamine N-oxide (CID 1145)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=1145 [cited 10 Feb 2014] .

[17]Tang, *et al.*, "Intestinal Microbial Metabolism of Phsophatidylcholine and Cardiovascular Risk," *New England Journal of Medicine*, Vol. 368, 2013, pp. 1575-1584.

[18]Wang, *et al.*, "Gut flora metabolism of phosphotidylcholine promotes cardiovascular disease," *Nature*, Vol. 472, No. 7341, 2011, pp. 57-63.

[19]Wipf, P., Belikova, N. A., Jiang, J., Pierce, J., Greenberger, J., Epperly, M., and Kagan, V., "Use of targeted nitroxide agents in preventing, mitigating and treating radiation injury," *US Patent and Trademark Office*, Patent Application No. 20110172214, 2011.

[20]The Metabolomics Innovation Center (TMIC), "Urea (HMDB00294) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00294, [cited 10 Feb 2014].

[21]National Center for Biotechnology Information (NCBI), "Urea (CID 1176)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=1176 [cited 10 Feb 2014] .

[22]The Metabolomics Innovation Center (TMIC), "Myoinositol (HMDB00211) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00211, [cited 11 Feb 2014].

[23]National Center for Biotechnology Information (NCBI), "Myoinositol (CID 892)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=892 [cited 11 Feb 2014] .
[24]The Metabolomics Innovation Center (TMIC), "Allantoin (HMDB00462) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00462, [cited 11 Feb 2014].
[25]National Center for Biotechnology Information (NCBI), "Allantoin (CID 892)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=892 [cited 11 Feb 2014] .
[26]Stewart, L. H., Trunkey, D., and Rebagliati, G. S., "Emergency Medicine in Space," *The Journal of Emergency Medicine*, Vol. 32, No. 1, 2007, pp. 45-54.
[27] Gontcharov, I. B., *et al.*, "Short communication: medical care system for NASA-Mir spaceflights," *Aviation and Space Medicine*, Vol. 73, 2002, pp. 1219-1223.
[28]The Metabolomics Innovation Center (TMIC), "Creatinine (HMDB00562) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00562, [cited 11 Feb 2014].
[29]National Center for Biotechnology Information (NCBI), "Creatinine (CID 588)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=588 [cited 11 Feb 2014] .
[30]The Metabolomics Innovation Center (TMIC), "Pyroglutamic acid (HMDB00267) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00267, [cited 11 Feb 2014].
[31]National Center for Biotechnology Information (NCBI), "Pyroglutamic acid (CID 7405)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=7405 [cited 11 Feb 2014] .
[32]Hsu, *et al*., "Treatment of antibiotic-resistant bacteria infection," *USPTO Patent Full-Text and Image Database*, US Patent No. 8,211,909, 2012.
[33]Buckman, B., *et al.*, "Novel inhibitors of Hepatitis C virus replication," *US Patent and Trademark Office*, Patent Application No. 20110312996, 2011.
[34]The Metabolomics Innovation Center (TMIC), "Trigonelline (HMDB00875) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00875, [cited 15 Feb 2014].
[35]National Center for Biotechnology Information (NCBI), "Trigonelline (CID 5570)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5570 [cited 15 Feb 2014] .
[36]Zhou, J., Chan, L., and Zhou, S., "Trigonelline: a plant alkaloid with therapeutic potential for diabetes and central nervous system disease," *Current Medicinal Chemistry*, Vol. 19, No. 21, 2012, pp. 3523-3531.
[37]Yoshinari, O., Takenake, A., and Igarashi, K., "Trigonelline ameliorates oxidative stress in type 2 diabetes Goto-Kakizaki rats," *Journal of Medicinal Food*, Vol. 16, No. 1, 2013, pp. 34-41.
[38]Ghule, A. E., Jadhav, S. S., and Bodhankar, S. L., "Trigonelline ameliorates diabetic hypertensive nephopathy by suppression of oxidative stress in kidney and reduction in renal cell apoptosis and fibrosis in streptozotocin induced neonatal diabetic (nSTZ) rats," *International Immunopharmacology*, Vol. 14, No. 4, 2012, pp. 740-748.
[39]The Metabolomics Innovation Center (TMIC), "3-aminoisobutanoic acid (HMDB03911) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb03911, [cited 17 Feb 2014].
[40]National Center for Biotechnology Information (NCBI), "3-aminoisobutyric acid (CID 64956)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=64956 [cited 17 Feb 2014] .
[41]Nielson, H. R., Sjolin, K. E., Nyholm, K., Baliga, B. S., Wong, R., and Borek, E., "Beta-aminoisobutyric acid, a new probe for the metabolism of DNA and RNA in normal and tumorous tissue," *Cancer Research*, Vol. 34, No. 6, 1974, pp. 1381-1384.
[42]Lee, Y. B., Kim, D. J., and Ahn, C. H., "Polymeric systems for the delivery of anticancer drugs," *US Patent and Trademark Office*, US Patent Application No. 20110086111, 2011.
[43]Matier, W. L., and Patil, G., "Amelioration of cataracts, macular degeneration and other ophthalmic diseases," *USPTO Patent Full-Text and Image Database*, US Patent No. 7,825,134, 2010.
[44]The Metabolomics Innovation Center (TMIC), "3-methylhistidine (HMDB00479) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00479, [cited 17 Feb 2014].
[45]National Center for Biotechnology Information (NCBI), "3-methylhistidine (CID 64969)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=64969 [cited 17 Feb 2014].
[46]Elia, M., Carter, A., Bacon, S., Winearls, C. G., and Smith, R., "Clinical usefulness of urinary 3-methylhistidine excretion in indicating muscle protein breakdown," *British Medical Journal*, Vol. 282, No. 6261, 1981, pp. 351-354.
[47]Long, C. L., Birkahn, R. H., Geiger, J. W., Betts, J. E., Schiller, W. R., and Blakemore, W. S., "Urinary excretion of 3-methylhistidine: an assessment of muscle protein catabolism in adult normal subjects and during malnutrition, sepsis, and skeletal trauma," *Metabolism*, Vol. 30, No. 8, 1981, pp. 765-776.
[48]Metametrix Clinical Laboratory, "Interpretive Guide for Amino Acids," *Laboratory Evaluations in Molecular Medicine*, Duluth, GA, 2014.
[49]The Metabolomics Innovation Center (TMIC), "creatine (HMDB00064) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00064, [cited 18 Feb 2014].
[50]National Center for Biotechnology Information (NCBI), "creatine (CID 586)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=586 [cited 18 Feb 2014].
[51]Kedia, A. W., Hofheins, J. E., Habowski, S. M., Ferrando, A. A., Gothard, M. D., and Lopez, H. L., "Effects of a Pre-workout Supplement on Lean Mass, Muscular Performance, Subjective Workout Experience and Biomarkers of Safety," *International Journal of Medical Sciences*, Vol. 11, No. 2, 2014, pp. 116-126.

[52]Candow, D. G., *et al.*, "Comparison of creatine supplementation before versus after supervised resistance training in healthy older adults," *Research in Sports Medicine*, Vol. 22, No. 1, 2014, pp. 61-74.
[53]Williams, J., Abt, D., and Kilding, A. E., "Effects of Creatine Monohydrate Supplementation on Simulated Soccer Performance," *International Journal of Sports Physiology and Performance*, 2014.
[54]The Metabolomics Innovation Center (TMIC), "glycine (HMDB00123) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00123, [cited 18 Feb 2014].
[55]National Center for Biotechnology Information (NCBI), "glycine (CID 750)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=750 [cited 18 Feb 2014].
[56]Hazardous Substances Data Bank (HSDB), "Glycine (CASRN: 56-40-6)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+56-40-6, [cited 19 Feb 2014].
[57]Household Products Database, "Glycine, (CAS: 56-40-6)" *US Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=56-40-6&tbl=TblChemicals&prodcat=all, [cited 19 Feb 2014].
[58]The Metabolomics Innovation Center (TMIC), "guanidoacetic acid (HMDB00128) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00128, [cited 19 Feb 2014].
[59]National Center for Biotechnology Information (NCBI), "guanidoacetic acid (CID 763)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=763 [cited 19 Feb 2014].
[60]Ostojic, S. M., Niess, B., Stojanovic, M., and Obrenovic, M., "Creatine metabolism and safety profiles after six-week oral guanidoacetic acid administration in healthy humans," *International Journal of Medical Sciences*, Vol. 10, No. 2, 2013, pp. 141-147.
[61]Borsook, M. E., and Borsook, H., "Treatment of cardiac decompensation with betaine and glycocyamine," *Annual Western Journal of Medicine and Surgery*, Vol. 5, 1951, pp. 830-835.
[62]Higgins, A. R., *et al.*, "Effects of creatine precursors in arthritis; clinical and metabolic study of glycocyamine and betaine," *California Medicine*, Vol. 77, 1952, pp. 14-18.
[63]Dixon, H. H., *et al.*, "Therapy in anxiety states and anxiety complicated by depression," *Western Journal of Surgical Obstetrics and Gynecology*, Vol. 62, 1954, pp. 338-341.
[64]National Center for Biotechnology Information (NCBI), "hippuric acid (CID 464)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=464 [cited 20 Feb 2014].
[65]Beyoğlu, D., and Idle, J. R., "The glycine deportation system and its pharmacological consequences," *Pharmacology and Therapeutics*, Vol. 135, No. 2, 2012, pp. 151-167.
[66]The Metabolomics Innovation Center (TMIC), "Hippuric acid (HMDB00714) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00714, [cited 20 Feb 2014].
[67]Krupp, D., Doberstein, N., Shi, L., and Remer, T., "Hippuric acid in 24-hour urine collections is a potential biomarker for fruit and vegetable consumption in healthy children and adolescents," *Journal of Nutrition*, Vol. 142, No. 7, 2012, pp. 1314-1320.
[68]Maggi, F., and Daly, E., "Use of human urine as a fertilizer for corn, potato, and soybean: a case-study analysis using a reactive model," *20th International Congress on Modeling and Simulation,* Adelaide, Australia, 2013.
[69]The Metabolomics Innovation Center (TMIC), "L-Alanine (HMDB00161) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00161, [cited 20 Feb 2014].
[70]National Center for Biotechnology Information (NCBI), "L-Alanine (CID 5950)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5950 [cited 20 Feb 2014].
[71]Chuang, J. C., Yu, C. L., and Wang, S. R., "Modulation of human lymphocyte proliferation by amino acids," *International Archive of Allergy and Applied Immunology*, Vol. 81, No. 1, 1990, pp. 173-176.
[72]The Metabolomics Innovation Center (TMIC), "L-Aspartic acid (HMDB00191) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00191, [cited 20 Feb 2014].
[73]National Center for Biotechnology Information (NCBI), "L-Aspartic acid (CID 5960)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5960 [cited 20 Feb 2014].
[74]Floersheim, G. L., Chiodetti, N., and Bieri, A., "Differential radioprotection of bone marrow and tumour cells by zinc aspartate," *The British Journal of Radiology*, Vol. 61, No. 726, 1988, pp. 501-508.
[75]Floersheim, G. L. and Floersheim, P., "Protection against ionizing radiation and synergism with thiols by zinc aspartate," *The British Journal of Radiology*, Vol. 59, No. 702, 1986, pp. 597-602.
[76]The Metabolomics Innovation Center (TMIC), "L-Cysteine (HMDB00574) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00574, [cited 20 Feb 2014].
[77]National Center for Biotechnology Information (NCBI), "L-Cysteine (CID 5862)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5862 [cited 20 Feb 2014].
[78]Hazardous Substances Data Bank (HSDB), "L-Cysteine (CASRN: 52-90-4)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+52-90-4, [cited 20 Feb 2014].
[79]The Metabolomics Innovation Center (TMIC), "L-Cystine (HMDB00192) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00192, [cited 20 Feb 2014].
[80]National Center for Biotechnology Information (NCBI), "L-Cystine (CID 67678)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=67678 [cited 20 Feb 2014].
[81]Medina, M. A., "Glutamine and Cancer," *The Journal of Nutrition*, Vol. 131, No. 9, 2001, pp. 25395-25425.

[82]The Metabolomics Innovation Center (TMIC), "L-Glutamine (HMDB00641) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00641, [cited 20 Feb 2014].
[83]National Center for Biotechnology Information (NCBI), "L-Glutamine (CID 5961)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5961 [cited 20 Feb 2014].
[84]Miller, A. L., "Therapeutic considerations of L-glutamine: a review of the literature," *Alternative Medicine Review: A Journal of Clinical Therapeutics*, Vol. 4, No. 4, 1999, pp. 239-248.
[85]Rajagopalan, K. N., and DeBerardinis, R. J., "Role of Glutamine in Cancer: Therapeutic and Imaging Implications," *The Journal of Nuclear Medicine*, Vol. 52, No. 7, 2011, pp. 1005-1008.
[86]The Metabolomics Innovation Center (TMIC), "L-Histidine (HMDB00177) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00177, [cited 21 Feb 2014].
[87]National Center for Biotechnology Information (NCBI), "L-Histidine (CID 6274)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=6274 [cited 21 Feb 2014].
[88]Nakazawa, S., *et al.*, "Histamine synthesis is required for granule maturation in murine mast cells," *European Journal of Immunology*, Vol. 44, No. 1, 2014, pp. 204-214.
[89]Neumann, D., Schneider, E. H., and Seifert, R., "Analysis of histamine receptor knockout mice in models of inflammation," *Journal of Pharmacology and Experimental Therapeutics*, Vol. 348, No. 1, 2014, pp. 2-11.
[90]Hazardous Substances Data Bank (HSDB), "L-Histidine (CASRN: 71-00-1)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+71-00-1, [cited 21 Feb 2014].
[91]The Metabolomics Innovation Center (TMIC), "L-Lysine (HMDB00182) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00182, [cited 21 Feb 2014].
[92]National Center for Biotechnology Information (NCBI), "L-Lysine (CID 5962)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5962 [cited 21 Feb 2014].
[93]Civitelli, R., Villareal, D. T., Agnusdei, D., Nardi, P., Avioli, L. V., and Gennari, C., "Dietary L-lysine and calcium metabolism in humans," *Nutrition*, Vol. 8, No. 6, 1992, pp. 400-405.
[94]Warwicker, K., Charonis, S., and Curtis, R. A., "Lysine and arginine content of proteins: computational analysis suggests a new tool for solubility design," *Molecular Pharmacology*, Vol. 11, No. 1, 2014, pp. 294-303.
[95]Sundar, S., Chen, Y, and Tong, Y. W., "Delivery of Therapeutics and Molecules using Self-Assembled Peptides," *Current Medicinal Chemistry*, 2013.
[96]The Metabolomics Innovation Center (TMIC), "L-Serine (HMDB00187) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00187, [cited 22 Feb 2014].
[97]National Center for Biotechnology Information (NCBI), "L-Serine (CID 5951)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5951 [cited 22 Feb 2014].
[98]Hazardous Substances Data Bank (HSDB), "L-Serine (CASRN: 56-45-1)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+56-45-1, [cited 22 Feb 2014].
[99]De Koning, T. J., Snell, K., Duran, M., Berger, R., Poll-The, B. T., and Surtees, R., "L-Serine in disease and development," *Biochemistry Journal*, Vol. 371, No. 3, 2003, pp. 653-661.
[100]The Metabolomics Innovation Center (TMIC), "L-Threonine (HMDB00167) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00167, [cited 22 Feb 2014].
[101]National Center for Biotechnology Information (NCBI), "L-Threonine (CID 6288)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=6288 [cited 22 Feb 2014].
[102]Hazardous Substances Data Bank (HSDB), "L-Threonine (CASRN: 72-19-5)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+72-19-5, [cited 22 Feb 2014].
[103]The Metabolomics Innovation Center (TMIC), "Phenylacetylglutamine (HMDB06344) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb06344, [cited 22 Feb 2014].
[104]National Center for Biotechnology Information (NCBI), "Phenylacetylglutamine (CID 92258)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=92258 [cited 22 Feb 2014].
[105]Zimmerman, L., Egestad, B., Jörnvall, H., and Bergström, J., "Identification and determination of phenylacetylglutamine, a major nitrogenous metabolite in plasma of uremic patients," *Clinical Nephrology*, Vol. 32, No. 3, 1989, pp. 124-128.
[106]Mokhtarani, M., *et al*., "Urinary phenylacetylglutamine as dosing biomarker for patients with urea cycle disorders," *Molecular Genetics and Metabolism*, Vol. 107, No. 3, 2012, pp. 308-314.
[107]Sherwood, L., "Human Physiology: From Cells to Systems," Cengage Learning, 2012.
[108]MacDonald, I. A., "Dietary strategies for the management of cardiovascular risk: role of dietary carbohydrates," *Proceedings of the Nutrition Society*, Vol. 21, 2014, pp. 1-5.
[109]Lucas, R., *et al.*, "Effects of sugar functional groups, hydrophobicity and fluorination on carbohydrate-DNA stacking interactions in water," *Journal of Organic Chemistry*, 2014.
[110]The Metabolomics Innovation Center (TMIC), "Arabitol (HMDB01851) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb01851, [cited 23 Feb 2014].
[111]National Center for Biotechnology Information (NCBI), "Arabitol (CID 439255)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=439255 [cited 23 Feb 2014].
[112]Lehtonen, L., *et al*., "Diagnosis of disseminated candidiasis by measurement of urine D-arabinitol/L-arabinitol ratio," *Journal of Clinical Microbiology*, Vol. 34, No. 9, 1996, pp. 2175-2179.

[113]Hayes, C., "The effect of non-cariogenic sweeteners on the prevention of dental caries: a review of the evidence," *Journal of Dental Education*, Vol. 65, No. 10, 2001, pp. 1106-1109.

[114]The Metabolomics Innovation Center (TMIC), "D-Galactose (HMDB00143) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00143, [cited 23 Feb 2014].

[115]National Center for Biotechnology Information (NCBI), "D-Galactose (CID 439357)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=439357 [cited 23 Feb 2014].

[116]Hazardous Substances Data Bank (HSDB), "Carrageenan Gum (CASRN: 9000-07-01)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~UfK8zR:1, [cited 23 Feb 2014].

[117]The Metabolomics Innovation Center (TMIC), "D-Glucose (HMDB00122) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00122, [cited 23 Feb 2014].

[118]National Center for Biotechnology Information (NCBI), "D-Glucose (CID 5793)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=5793 [cited 23 Feb 2014].

[119]The Metabolomics Innovation Center (TMIC), "D-Threitol (HMDB04136) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb04136, [cited 23 Feb 2014].

[120]National Center for Biotechnology Information (NCBI), "D-Threitol (CID 169019)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=169019 [cited 23 Feb 2014].

[121]The Metabolomics Innovation Center (TMIC), "D-Xylose (HMDB00098) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00098, [cited 23 Feb 2014].

[122]National Center for Biotechnology Information (NCBI), "D-Xylose (CID 135191)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=135191 [cited 23 Feb 2014].

[123]Ohkohchi, N., Himukai, M., Igarashi, Y., and Kasai, M., "Mechanism of D-xylose transport in human small intestine," *Journal of Pediatric Gastroenterology and Nutrition*, Vol. 5, No. 3, 1986, pp. 372-378.

[124]Kurtzman, C. P., "Biology and physiology of the D-xylose fermenting yeast *Pachysolen tannophilus*," *Advances in Biochemical Engineering/Biotechnology*, Vol. 27, 1983, pp. 73-83.

[125]Cadete, R.M, *et al.*, "Diversity and physiological characterization of D-xylose-fermenting yeasts isolated from the Brazilian Amazonian Forest," *PLoS One*, Vol. 7, No. 8, 2012.

[126]The Metabolomics Innovation Center (TMIC), "Erythritol (HMDB02994) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb02994, [cited 23 Feb 2014].

[127]National Center for Biotechnology Information (NCBI), "Erythritol (CID 222285)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=222285 [cited 23 Feb 2014].

[128]The Metabolomics Innovation Center (TMIC), "Gluconic acid (HMDB00625) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00625, [cited 23 Feb 2014].

[129]National Center for Biotechnology Information (NCBI), "Gluconic acid (CID 10690)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=10690 [cited 23 Feb 2014].

[130]Household Products Database, "Gluconic acid (CASRN: 000133-42-6)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=133-42-6&tbl=TblChemicals&prodcat=all, [cited 23 Feb 2014].

[131]The Metabolomics Innovation Center (TMIC), "Glycerol (HMDB00131) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00131, [cited 23 Feb 2014].

[132]National Center for Biotechnology Information (NCBI), "Glycerol (CID 753)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=753 [cited 23 Feb 2014].

[133]Household Products Database, "Glycerol (CASRN: 56-81-5)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=56-81-5&tbl=TblChemicals&prodcat=all, [cited 23 Feb 2014].

[134]The Metabolomics Innovation Center (TMIC), "Lactose (HMDB00186) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00186, [cited 23 Feb 2014].

[135]National Center for Biotechnology Information (NCBI), "Lactose (CID 84571)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=84571 [cited 23 Feb 2014].

[136]Household Products Database, "Lactose (CASRN: 63-42-3)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=63-42-3&tbl=TblChemicals&prodcat=all, [cited 23 Feb 2014].

[137]The Metabolomics Innovation Center (TMIC), "Mannitol (HMDB00765) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00765, [cited 23 Feb 2014].

[138]National Center for Biotechnology Information (NCBI), "Mannitol (CID 6251)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=6251 [cited 23 Feb 2014].

[139]The Metabolomics Innovation Center (TMIC), "Acetic acid (HMDB00042) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00042, [cited 24 Feb 2014].

[140]National Center for Biotechnology Information (NCBI), "Acetic acid (CID 176)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=176 [cited 24 Feb 2014].

[141]Raspor, P. and Goranovic, D., "Biotechnological applications of acetic acid bacteria," *Critical Reviews in Biotechnology*, Vol. 28, No. 2, 2008, pp. 101-124.

[142]Household Products Database, "Acetic acid (CASRN: 64-19-7)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=64-19-7&tbl=TblChemicals&prodcat=all, [cited 24 Feb 2014].

[143]The Metabolomics Innovation Center (TMIC), "Citric acid (HMDB00094) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00094, [cited 24 Feb 2014].

[144]National Center for Biotechnology Information (NCBI), "Citric acid (CID 311)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=311 [cited 24 Feb 2014].

[145]Pignatelli, P., *et al.*, "Acid citrate dextrose (ACD) formula A as a new anticoagulant in the measurement of in vitro platelet aggregation," *Journal of Clinical Laboratory Analysis*, Vol. 9, No. 2, 1995, pp. 138-140.

[146]Household Products Database, "Citric acid (CASRN: 77-92-9)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=77-92-9&tbl=TblChemicals&prodcat=all, [cited 24 Feb 2014].

[147]The Metabolomics Innovation Center (TMIC), "Formic acid (HMDB00142) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00142, [cited 24 Feb 2014].

[148]National Center for Biotechnology Information (NCBI), "Formic acid (CID 284)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=284 [cited 24 Feb 2014].

[149]Household Products Database, "Formic acid (CASRN: 64-18-6)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=64-18-6&tbl=TblChemicals&prodcat=all, [cited 24 Feb 2014].

[150]The Metabolomics Innovation Center (TMIC), "Glycolic acid (HMDB03035) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb03035, [cited 24 Feb 2014].

[151]National Center for Biotechnology Information (NCBI), "Glycolic acid (CID 757)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=757 [cited 24 Feb 2014].

[152]Household Products Database, "Glycolic acid (CASRN: 79-14-1)," *U.S. Department of Health and Human Services*, URL: http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=79-14-1&tbl=TblChemicals&prodcat=all, [cited 24 Feb 2014].

[153]The Metabolomics Innovation Center (TMIC), "L-Lactic acid (HMDB00190) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00190, [cited 24 Feb 2014].

[154]National Center for Biotechnology Information (NCBI), "L-Lactic acid (CID 107689)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=107689 [cited 24 Feb 2014].

[155]Hazardous Substances Data Bank, "Lactic acid (CASRN: 50-21-5)," *National Library of Medicine*, URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+50-21-5, [cited 24 Feb 2014].

[156]Surenkok, O., Kin-Isler, A., Aytar, A., and Gültekin, Z., "Effect of trunk-muscle fatigue and lactic acid accumulation on balance in healthy subjects," *Journal of Sports Rehabilitation*, Vol. 14, No. 4, 2008, pp. 380-386.

[157]Rachoin, J. S., Weisberg, L. S., and McFadden, C. B., "Treatment of lactic acidosis: appropriate confusion," *Journal of Hospital Medicine*, Vol. 5, No. 4, 2010, pp. E1-17.

[158]The Metabolomics Innovation Center (TMIC), "Taurine (HMDB00251) Metabocard," *The Human Metabolome Database (HMDB)*, Version 3.5, URL: http://www.hmdb.ca/metabolites/hmdb00251, [cited 24 Feb 2014].

[159]National Center for Biotechnology Information (NCBI), "Taurine (CID 1123)," *PubChem Compound Summary*, URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=1123 [cited 24 Feb 2014].

[160]Sperelakis, N., Satoh, H., and Bkaily, G., "Taurine effects on ionic currents in myocardial cells," *Advances in Experimental Medicine and Biology*, Vol. 135, 1992, pp. 129-143.