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Guidance on Potassium from Water Softeners

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Federal-Provincial-Territorial Committee on
Drinking Water

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Other documents concerning Canadian drinking water quality can be found on the following Web page: http://www.healthcanada.gc.ca/waterquality.

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Background on guidance documents

The main role of the Federal-Provincial-Territorial Committee on Drinking Water is the development of the Guidelines for Canadian Drinking Water Quality. This role has evolved over the years, and new methodologies and approaches have led the Committee to develop a new type of document, Guidance documents, to provide advice and guidance on issues related to drinking water quality for parameters that do not require a formal Guideline for Canadian Drinking Water Quality.

There are two instances when the Federal-Provincial-Territorial Committee on Drinking Water may choose to develop guidance documents. The first would be to provide operational or management guidance related to specific drinking water related issues (such as boil water advisories), in which case the documents would provide only limited scientific information or health risk assessment.

The second instance would be to make risk assessment information available when a guideline is not deemed necessary. The Federal-Provincial-Territorial Committee on Drinking Water establishes the Guidelines for Canadian Drinking Water Quality specifically for contaminants that meet all of the following criteria:

1. exposure to the contaminant could lead to adverse health effects;
2. the contaminant is frequently detected or could be expected to be found in a large number of drinking water supplies throughout Canada; and
3. the contaminant is detected, or could be expected to be detected, at a level that is of possible health significance.

If a contaminant of interest does not meet all these criteria, the Federal-Provincial-Territorial Committee on Drinking Water may choose not to establish a numerical guideline or develop a Guideline Technical Document. In that case, a guidance document may be developed.

Guidance documents undergo a similar process as Guideline Technical Documents, including public consultations through the Health Canada Web site. They are offered as information for drinking water authorities, and in some cases to help provide guidance in spill or other emergency situations.

Part A - Guidance on potassium from water softeners

Although potassium may cause some health effects in susceptible individuals, potassium intake from drinking water is well below the level at which adverse health effects may occur. Health concerns would be related to the consumption of drinking water treated by water softeners using potassium chloride, affecting only individuals with kidney dysfunction or taking medications that interfere with normal potassium-dependent functions in the body. It is recommended that susceptible individuals avoid the consumption of water treated by water softeners using potassium chloride.

Potassium is an essential element in humans, and is not found in drinking water at levels that could be a concern to human health. However, the consumption of drinking water treated by water softeners using potassium chloride may significantly increase exposure to potassium. This is not a concern for the general population. However, increased exposure to potassium could result in significant health effects in people with kidney disease or other conditions, such as heart disease, coronary artery disease, hypertension, diabetes, and who are taking medication that interfere with normal body potassium handling.

Potassium plays a critical role in many vital cell functions, such as metabolism, growth, repair and volume regulation, as well as in the electric properties of the cell. Adverse health effects from exposure to potassium in drinking water are unlikely in healthy individuals. Higher than normal potassium concentrations in the blood (hyperkalemia) and ensuing health effects are unlikely because potassium is rapidly excreted in the absence of pre-existing kidney damage.

However, potassium levels in drinking water from water softeners using potassium chloride can be very high, and may significantly increase an individual's intake of potassium that could cause hyperkalemia in susceptible individuals. As a consequence, people with certain medical conditions (and medications) that potentially cause hyperkalemia should avoid the consumption of water (for drinking or cooking) from water softeners using potassium chloride.

Potassium is a natural and essential element in plants and animals, and humans are exposed to it primarily through food, at levels unlikely to pose health risks. In Canada, the total average intake of potassium from all sources is approximately 3.1 g/day for a 70 kg adult, well below the Adequate Intake set at 4.7 g/day for adults. Municipally treated drinking water may contain small concentrations of potassium. The use of a water softeners using potassium chloride can significantly increase the levels of potassium in drinking water, even at water hardness levels considered to be acceptable.

In cases where potassium is added to water through the use of a water softener, the recommended strategy is to limit or prevent the addition of potassium to water that will be ingested. This can be done by having a proportion of the water bypass the softener altogether. Although removal technologies are available to remove potassium, they are generally more expensive and redundant when combined with the softening treatment.

Part B - Supporting information

B.1 Physical/environmental considerations and exposure

Potassium (CAS No. 7440-09-7) is a alkali metal and the seventh most common element on earth (Lewis, 1997). It comprises 2.59% of the Earth's crust, is highly reactive and does not occur in nature as a free metal (Burkhardt and Brüning, 2002). Potassium has a crystal structure, has high thermal and electrical conductivities (Burkhardt and Brüning, 2002) and is rapidly oxidized in moist air (Lewis, 1997). It has a melting point of 63.5°C, a boiling point of 759°C and a density of 0.89 g/cm^3 at 20°C (Lide, 2004).

Potassium's principal salt, potassium chloride (CAS No. 7447-40-7), readily dissolves in water (34.4 g/100 g at 20°C), has a low vapour pressure (0.13 kPa at 865°C) (Linke, 1965) and a low octanol/water partition coefficient (log K_{ow}) of -0.46 (OECD, 2001). Potassium chloride is odourless and has a taste detection threshold of 0.32 g/100 mL (Environment Canada, 1985).

Potassium is a natural and essential element in plants and animals. Humans are primarily exposed to potassium through food. Although potassium concentrations in drinking water are generally low and do not pose health concerns, the high water solubility of potassium chloride and its use in water softeners can lead to significantly increased exposure.

B.1.1 Water

The concentration of potassium in seawater is 0.38 g/L. Both sea salt aerosols and soil dust can contribute to the potassium content of rainwater. Potassium concentrations in rainwater are generally low, with an average annual concentration of just over 0.1 mg/L (NRCC, 1977).

Potassium levels in deep bedrock aquifers of the prairies tend to be higher and are generally a function of depth below surface and the distance from the outcrop area containing the potassium minerals (NRCC, 1977). In Saskatchewan, potash formations are very deep and are hydrogeologically isolated from useable groundwater resources by very thick layers of low-permeability shales (Shaheen, 2004).

Generally, potassium levels in Canadian lakes and rivers are less than 10 mg/L: Cordilleran regions (Fraser, Columbia, Yukon, Peace, Oldman, Powell rivers), 0.2–1.3 mg/L; interior plains region (Saskatchewan, Mackenzie, Nelson rivers), 0.6–8.2 mg/L; Canadian Shield region (Coppermine, Great Whale), 0.1–0.6 mg/L; central Great Lakes (Lake Ontario), 1.9–2.7 mg/L; Ottawa and St. Lawrence rivers, 0.9–1.2 mg/L; and Canadian Appalachian Region (rivers), 0.3–1.1 mg/L (NRCC, 1977).

Provincial monitoring data (Table 1) for treated and raw drinking water (surface water and groundwater) indicate that average potassium concentrations in drinking water generally range from <1.0 to 8.0 mg/L.

Table 1: Concentrations of potassium in drinking water in Canada

Location and period	Range of potassium concentrations in drinking water (mg/L)	Average potassium concentrations in drinking water (mg/L)	Reference
Alberta (1990–2004)	0.1– 43	3.9 (n = 3700)	Alberta Environment, 2004
Newfoundland and Labrador (2000–2004)	0.27–25.3	1.1 (n = 3818)	Newfoundland and Labrador Department of Environment and Conservation, 2004
Nova Scotia (1975–2001)	<0.1–10	0.9 (n = 3132)	Nova Scotia Department of Environment and Labour, 2004
Ontario (1999–2004)	0.05–20	1.6 (n = 5792)	Ontario Ministry of the Environment, 2004
Saskatchewan (1985–2002)	0.13–30	7.8 (n = 133)	Saskatchewan Department of Environment, 2004
Saskatchewan (1963–2003)	0.05–51	8.0 (n = 2187)	Saskatchewan Department of Environment, 2004
Yukon (1996–2003)	<0.01–3.6	1.6 (n = 44)	Yukon Department of Health and Social Services, 2004

Potassium permanganate may also be used in the drinking water treatment process. It is a strong oxidant which can be used in municipal treatment plants to control iron, manganese and other parameters. Resulting levels of potassium in drinking water are relatively low when compared to levels resulting from water softeners using potassium chloride.

Estimated contribution from municipal drinking water

The average intake of potassium from food, beverages and drinking water for Canadian adults (n = 18 214, 19–71+ years) from surveys conducted between 1990 and 1999 in 10 provinces ranged from 3.3 to 3.6 g/day for men and from 2.6 to 2.7 g/day for women. The 5^{th} and 95^{th} percentiles of intake were 1.69 g/day and 4.67 g/day, respectively, and the average intake for all individuals was 3.1 g/day or 44 mg/kg bw per day, based on a 70-kg adult (IOM, 2005).

Using the highest average potassium concentration of 8 mg/L from Table 1 (range <1.0–8.0 mg/L), an estimated intake of potassium from drinking water of 0.20 mg/kg bw per day can be calculated for a 70-kg adult consuming 1.5 L of drinking water per day. This estimate is less than 1% of the average total daily intake for potassium (44 mg/kg bw per day).

Water softeners

Water softeners remove minerals such as calcium and magnesium ions from hard water, replacing them with either potassium or sodium ions, depending on whether potassium chloride or sodium chloride is used in the unit.

The intake of potassium from the consumption of drinking water treated with a water softener using potassium chloride will vary depending on the level of hardness. Assuming that a potassium chloride water softener emits 14 mg K^+/L in water with a hardness of 17 mg $CaCO_3$/L, the amount of potassium emitted in 1 L of drinking water can be calculated for different hardness levels. Table 2 shows that a water softener using potassium chloride can add significantly to the intake of potassium when compared to the amount that Canadian adults typically consume in drinking water, even when the water treated had water hardness levels considered to be acceptable.

Table 2: Intake of potassium as a result of water softener use, by hardness level

Drinking water hardness (mg $CaCO_3$/L)	K^+ concentration (mg/L)	Intake[c] (mg/kg bw per day)
treated tap water	8.0[a]	0.2
100 (acceptable) [b]	82	1.8
200 (poor) [b]	164	3.5
500 (unacceptable) [b]	411	8.8

[a] Average K^+ concentration in drinking water, based on Saskatchewan levels in Table 1
[b] Based on Health Canada's drinking water quality guideline for hardness.
[c] Assuming consumption of 1.5 L of water per day by a 70-kg adult.

Strategies to reduce exposure

When potassium is added to the water by an ion exchange water softening treatment process, the recommended strategy is to limit or prevent the addition of potassium to water intended for human consumption. This can be done by having a proportion of the water bypass the softener altogether. Although removal technologies are available to remove potassium, they are generally more expensive and redundant when combined with the softening treatment.

B.1.2 Food

Food is the major source of potassium for the general population. The potassium contents of various food groups, in decreasing order, are as follows (in mg/100 kcal): leafy green vegetables, 1500; fruit of vine-based plants, 1200; root vegetables, 975; beans and peas, 500; tree fruits, 430; tubers, 400; milk and yogurt, 350; meats, 230; nuts, 110; eggs, 90; cereal grains, 90; and cheese, 50 (IOM, 2005). Therefore, the greater the amount of fruits and vegetables consumed, the higher the potassium intake of an individual.

In unprocessed foods, potassium occurs predominantly in association with bicarbonate-generating precursors such as citrate and, to a lesser extent, with phosphate. Potassium chloride is also used in processed foods and supplements (IOM, 2005).

B.2 Health information

B.2.1 Health considerations

Potassium is an essential element in plant, animal and human nutrition (Lewis, 1997). In humans, potassium ions play a critical role in many vital cell functions, such as metabolism, growth, repair and volume regulation, as well as in the electric properties of the cell (Adriogué and Wesson, 1994).

Essentiality

Total body potassium amounts to 3500 meq[1], with the majority (approximately 2700 meq, or 77%) being held within the skeletal muscle. The liver, bone and red blood cells each account for approximately 270 meq (Adriogué and Wesson, 1994).

Potassium is the major intracellular cation. Potassium that is administered either orally or intravenously must transit through the extracellular fluid compartment to get to the much larger intracellular reservoir of potassium. The concentration inside cells is approximately 150 mmol/L, whereas the plasma K^+ concentration normally ranges from 3.5 to 5.0 mmol/L (Braunwald et al., 2001). Since K^+ is the exclusive cation with substantial permeability across the cell membrane, it will accumulate within the cytosol, balancing the negative charge of phosphate (HPO_4^{2-}) and protein (Adriogué and Wesson, 1994). The ratio of intracellular fluid K^+ concentration to extracellular fluid K^+ concentration (normally 38:1) is the principal result of the resting membrane potential and is crucial for nerve impulse transmission, muscle contraction and heart function (Braunwald et al., 2001; Higdon, 2004).

Specific enzymes require potassium, including cell Na^+, K^+-ATPase, which actively pumps K^+ in and Na^+ out of the cell in a 2:3 ratio and is responsible for generating the resting membrane potential (Braunwald et al., 2001). Another enzyme, pyruvate kinase, helps the body convert blood sugar into glycogen (Woodford, 2003; Higdon, 2004).

Potassium also plays a key role in mediating the osmotic balance of the body fluids and is involved in the regulation of the acid–base balance of the body by affecting the kidney's ability to reabsorb bicarbonate — the main extracellular buffer to metabolic acids (OECD, 2001, Brandis 2005).

The adequate intake for adults (19–70+ years of age) is 4.7 g/day (67 mg/kg bw/day for a 70 kg adult) and is based on potassium's effect of countering salt (sodium chloride) sensitivity in African Americans, as well as epidemiological evidence linking higher levels of potassium intake with decreased risk of bone loss and kidney stones. A potassium intake level below 4.7 g/day is recommended for those individuals with kidney dysfunction. Due to a lack of data from dose–response trials, an estimated average requirement (recommended daily allowance) could not be established (IOM, 2005).

[1] 1 meq = 1 mmol = 39.1 mg K^+.

Absorption, distribution and excretion

Potassium intake is through ingestion and varies with the diet. Approximately 90% of intake of potassium is absorbed by the gastrointestinal tract. As ingested K^+ is absorbed and enters the portal circulation, it stimulates insulin release, which in turn initiates Na^+, K^+-ATPase pump activity and the rapid entry of potassium into cells. An insulin deficiency, in contrast, results in the movement of potassium from the intracellular to the extracellular fluid (Braunwald et al., 2001; Gennari, 2002).

Factors that affect the distribution of K^+ in the body include hormones, glucose and protein metabolism, acid–base balance, levels of other electrolytes, osmolality, cell turnover and drugs (Adriogué and Wesson, 1994; Braunwald et al., 2001).

In healthy individuals, excretion matches intake on a daily basis (Gennari, 2002). Renal excretion accounts for approximately 90–95% of K^+ intake, while the remaining 5–10% is excreted in the stools. Faecal K^+ normally amounts to 8–15 meq/day, but in diarrhoeal states it increases substantially and can reach 300 meq/day (Adriogué and Wesson, 1994). The amount of K^+ lost in the stool can also increase significantly in individuals with chronic renal disease (Braunwald et al., 2001). Excretion by sweat glands is usually minimal; however, if excessive sweating occurs, this extrarenal route can result in K^+ losses of up to 10–40 meq/day (Adriogué and Wesson, 1994).

The principal cells of the distal nephron in the kidney (late distal tubule and cortical, medullary and papillary collecting tubule) are responsible for most of the renal excretion of K^+ (Adriogué and Wesson, 1994). Several factors, including Na^+ absorption and the hormone aldosterone, regulate K^+ secretion (Gennari, 2002; IOM, 2005). Within 30 minutes of ingestion, a rise in the K^+ extracellular concentration stimulates the adrenal cortex to release aldosterone, which in turn increases the number and activity of K^+ pumps (Na^+, K^+-ATPase), which results in the excretion of K^+ in the distal nephron (Adriogué and Wesson, 1994; Gennari, 2002). Excretion of K^+ in the urine increases when the extracellular concentration is high and decreases when the concentration is low (Adriogué and Wesson, 1994).

B.2.2 Health effects

Health effects due to potassium consumption in drinking water are unlikely to occur in most individuals. Potassium intoxication by ingestion is rare, because potassium is rapidly excreted in the absence of pre-existing kidney damage and because large single doses usually induce vomiting (Gosselin et al., 1984). However, acute ingestion of doses greater than 2.0 meq/kg bw (>78 mg/kg bw or 5.5 g for a 70 kg adult) by individuals with normal kidney function can overwhelm homeostatic mechanisms and possibly cause death (Buckley et al., 1995).

Adverse effects due to higher than normal K^+ plasma concentrations (hyperkalemia) may occur in certain segments of the population when consuming drinking water from water softeners using potassium chloride. Individuals most at risk include those with kidney disease, as well as other conditions (heart disease, coronary artery disease, hypertension, diabetes) who are taking medication(s) that interfere with normal potassium-dependent functions in the body. Adverse effects may also occur when K^+ plasma concentrations are lower (hypokalemia) than the normal range (3.5–5.0 mmol/L). Both hyperkalemia and hypokalemia result from disruptions in transcellular homeostasis or in the renal regulation of K^+ excretion (Gennari, 2002).

Hyperkalemia

Hyperkalemia is defined as K^+ plasma concentrations greater than 5.0 mmol/L and may be precipitated in a number of clinical situations, including increased dietary intake (potassium chloride supplementation, water softeners using potassium chloride), haemorrhage, transfusion of stored red blood cells, metabolic acidosis, rhabdomyolysis and intake of medications that inhibit K^+ entry into cells (Braunwald et al., 2001). In the majority of cases, however, impaired kidney K^+ excretion is the main cause of hyperkalemia (Gennari, 2002). Factors that affect kidney function include age and the existence of medical conditions such as kidney and cardiovascular diseases, hypertension and type 1 and 2 diabetes (Perazella and Mahnensmith, 1997; Weir, 1997; Braunwald et al., 2001; IOM, 2005).

Typically, kidney mass decreases by approximately one-third from early adulthood to the eighth decade of life. This decrease is normally accompanied by reductions in renal blood flow, glomerular filtration rate and several tubular transport functions (Perazella and Mahnensmith, 1997). However, due to an increased elimination of K^+ via the remaining nephrons, by enhancing secretion and/or diminishing reabsorption, plasma concentrations of K^+ do not rise until the glomerular filtration rate falls to less than one-fourth of normal (Adriogué and Wesson, 1994; Braunwald et al., 2001).

When hyperkalemia occurs, it causes a partial depolarization of the cell membrane by altering the ratio of intracellular to extracellular fluid K^+ concentration, which in turn affects neural transmission, muscle contraction and blood vessel constriction (IOM, 2005). Prolonged depolarization reduces membrane excitability and results in weakness. This may progress to paralysis and hypoventilation if the respiratory muscles are involved. Hyperkalemia also impairs net acid excretion and results in metabolic acidosis, which may exacerbate hyperkalemia as a result of K^+ movement out of cells. The most serious effect is the depolarization of cardiac muscle and the potential for cardiac arrest (Braunwald et al., 2001). Patients with a serum K^+ greater than 6.0 meq/L are considered at risk for cardiac arrest (Gennari, 2002). However, death from cardiac arrest normally occurs at 10 to 12 meq/L but may take place at lower levels depending on whether the intracellular fluid K^+ concentration is severely depleted (HSDB, 2003).

In addition to neuromuscular, cardiovascular and renal effects, hyperkalemia also affects the endocrine system. Effects include the stimulation of the adrenal gland and pancreas and the secretion of aldosterone and insulin, respectively (Adriogué and Wesson, 1994).

Often, a disturbance in potassium excretion does not result in hyperkalemia until an intercurrent illness supervenes or some other perturbation in potassium homeostasis is imposed (Perazella and Mahnensmith, 1997). A case study reported in the scientific literature underlines this fact. It was indicated that an elderly man developed acute renal failure and hyperkalemia because he had consumed 3–4 L of water daily containing 274 mg K^+/L from a water softener using potassium chloride. Other contributing factors to the development of this condition were this individual's kidney disease, diabetes and medication taken for hypertension (Graves, 1998).

The consumption of drinking water from water softeners using potassium chloride on its own is unlikely to cause hyperkalemia. However, in combination with certain diseases and medications, it is possible that this condition may be precipitated. A number of medications can cause hyperkalemia when administered to individuals with kidney disease or diseases that affect potassium homeostatasis. These drugs can be divided into two categories: those that interfere

with the cellular mechanisms that regulate potassium uptake, and those that interfere with renal potassium excretion. The first category includes non-selective beta blockers, used in the treatment of hypertension, heart disease, coronary artery disease and fluid-retaining syndromes. The second category includes the following classes of drugs: potassium sparing diuretics (hypertension, heart disease, kidney and liver disease); nonsteroidal anti-inflamatory drugs (NSAIDs) (pain treatment); angiotensin-converting enzyme (ACE) inhibitors (heart disease, coronary artery disease, hypertension, diabetes, kidney disease); angiotensin II receptor blockers (heart disease, hypertension); trimethoprim (HIV treatment); cyclosporin (immunosuppresive drug) and aldosterone inhibitors (heart disease, hypertension, birth control) (Perazella and Mahnensmith, 1997; Perazella, 2000; CCS, 2003; CHS, 2005).

In Canada, it is estimated that approximately 44 000 individuals have stage 4 (15–30% of kidney function) and stage 5 (<15% of kidney function) kidney disease (Stigant et al., 2003) and are at greater risk of developing hyperkalemia under certain conditions, including potassium supplementation (KCl based water softener) and/or the consumption of certain medications. In order to guard against the potential for hyperkalemia, individuals who are on dialysis (stage 5 kidney disease) are normally restricted to a potassium intake of 2–3 g/day (28–43 mg/kg bw per day for a 70-kg adult) (Daugirdas et al., 2001).

It is important to note that potassium supplementation from water softeners using potassium chloride and the potential for hyperkalemia is not only a problem for people with kidney disease, but may also affect individuals who are taking multiple medications (described above) for the treatment of a single disease (i.e., hypertension). In addition, the population is aging and individuals often have more than one disease (including heart disease, hypertension, diabetes, arthritis) which increases the probability that individuals are on more than one of the above medications. As a consequence, the population at risk from potassium supplementation (water softeners using potassium chloride is significantly larger than simply those individuals with kidney disease. In addition, a trend towards greater obesity in the Canadian population in recent decades suggests that many of the diseases in question (Katzmarzyk, 2002) and the corresponding drug treatments will continue to pose a background of risk for hyperkalemia given unregulated inputs of potassium.

Hyperkalemia is unlikely to occur in healthy individuals, because of homeostasis and because the total average intake of potassium from all sources for Canadians approximates 44 mg/kg bw per day (3.1 g/day for a 70 kg adult). An acute exposure of 78 mg/kg bw (5.5 g for a 70 kg adult) would be required to precipitate hyperkalemia in individuals with normal renal function.

Hypokalemia

Hypokalemia is defined as a K^+ plasma concentration below 3.5 mmol/L. Since 98% of total body potassium is intracellular, the presence of this condition indicates significant total body potassium depletion (Fervenza and Rabkin, 2002) and is rarely seen in healthy adults. Hypokalemia is caused by one or more of the following: significant decreased net intake, transcellular shifts into cells or increased net loss (renal and extrarenal) (Braunwald et al., 2001). The most common cause of potassium depletion and hypokalemia is the use of diuretics (Gennari, 2002).

In the event of a significant potassium deficiency, the most severely affected systems and organs include the cardiovascular and neurological systems, muscles and kidney (Fervenza and Rabkin, 2002). Common symptoms include fatigue and muscular weakness of the lower extremities (Braunwald et al., 2001). Severe hypokalemia may lead to progressive weakness, hypoventilation, complete paralysis and cardiac arrest (Gennari, 2002). In the kidney, hypokalemia may lead to polyuria (higher passage of urine) and polydipsia (excessive thirst), and sustained potassium depletion can lead to hypokalaemic nephropathy (Fervenza and Rabkin, 2002). Other effects of hypokalemia include hypercalciuria, growth retardation, reductions in insulin secretion and alterations in carbohydrate metabolism (Adriogué and Wesson, 1994; IOM, 2005). Epidemiological studies have linked a low-potassium diet with an increased prevalence of hypertension among certain populations (see below).

Hypertension

Animal studies have indicated that potassium supplementation lowers blood pressure when some rat strains are exposed to high-sodium diets. Potassium depletion has also been found to produce variable results in terms of blood pressure, depending on the genetics, magnitude of potassium depletion and amount of sodium in an animal's diet (Sato et al., 1991; DiBona and Jones, 1992; Krishna, 1994; Tobian, 1997; Ray et al., 2001).

Some epidemiological studies have found an inverse association between blood pressure and potassium intake. However, blood pressure has been more closely associated with the ratio of sodium–potassium excretion than with the intake of either electrolyte alone (IOM, 2005).

In a meta-analysis of 33 randomized controlled trials investigating the effect of oral potassium in the treatment and prevention of hypertension in 2609 people (African American and white), 12 trials were conducted with non-hypertensives and 21 trials with hypertensives. There was a statistically significant ($p < 0.001$) reduction in systolic and diastolic blood pressure in 34% and 30% of trials, respectively. The mean systolic and diastolic blood pressure reductions were 3.1 mmHg and 2.0 mmHg, respectively. A subgroup analysis indicated a greater trend towards reductions in blood pressure as a result of potassium supplementation in African Americans and when sodium intake was high (Whelton et al., 1997).

The mechanism behind the antihypertensive effect of potassium is unclear. Several reasons have been suggested and include a vasodilation effect due to a direct or indirect action of potassium on vascular smooth muscle (Pamnani et al., 2000), an increase in the urinary excretion of sodium chloride in the renal tubule (IOM, 2005), a vasodepressor effect produced via Na^+, K^+-ATPase and the endocrine system (Pamnani et al., 2000) and potassium's complex interaction with several nutrients and substances (Suter, 1998).

It should also be noted that hypertension is a cause of kidney disease and therefore is a risk factor for hyperkalemia (Suter, 1998).

Stroke

Potassium has potential vascular protective properties. In animal studies, supplemented potassium citrate and potassium bicarbonate were found to reduce mortality from strokes and in some cases attenuate hypertension in different strains of rats. Potassium chloride, on the other hand, was found to increase hypertension and the risk of stroke (IOM, 2005).

In epidemiological studies, evidence of an inverse relationship between dietary potassium intake and stroke-associated mortality has been observed in several, but not all, cross-sectional and cohort studies after varying degrees of adjustment for potential confounders (IOM, 2005).

Based on an analysis of treatment and prevention trials, it was recommended that the daily intake of potassium should be 60 mmol (2.3 g) or more, because this level of intake has been associated with a reduced risk of stroke-related death (Burgess et al., 1999).

Genotoxicity

When *Salmonella typhimurium* strains were exposed in a bacterial reverse mutation assay to doses of potassium chloride with and without metabolic activation, there were no significant increases in mutation frequencies (Mortelmans et al., 1986). Results were also negative when *Escherichia coli* were exposed to potassium chloride in an SOS chromotest (Olivier and Marzin, 1987).

In mouse lymphoma mutation tests, potassium chloride was found to be weakly mutagenic at high concentrations: >7000 µg/plate without metabolic activation and >4000 µg/plate with metabolic activation (Mitchell et al., 1988; Myhr and Caspary, 1988). In Chinese hamster ovary cells at potassium chloride concentrations of 5500 and 6000 µg/plate, there were 19% and 28% aberrant cells, respectively. The authors concluded that increases in mutagenicity and chromosome aberrations were linked to the cytotoxicity caused by the high concentrations and that the mutagenic effect of potassium chloride was probably linked to the disruption of osmotic balance and a subsequent interference with chromosomal stability (Brusick, 1988; Seeberg et al., 1988).

Cancer

Potassium chloride is not classified as a carcinogen. The modifying effects of potassium chloride and sodium chloride ingestion on glandular stomach carcinogenesis were investigated in male Wistar rats induced by *N*-methyl-*N´*-nitro-*N*-nitrosoguanidine (MNNG). After initiation of treatment with MNNG at 100 mg/L in their drinking water, rats were fed a diet supplemented with 5% NaCl (approximately 2.5 g/kg bw per day, group 1), 2.5% NaCl (approximately 1.25 g/kg bw per day, group 2), 2.5% NaCl plus 2.5% KCl (approximately 1.25 g/kg bw per day each, group 3), 5% KCl (approximately 2.5 g/kg bw per day, group 4), 2.5% KCl (approximately 1.25 g/kg bw per day, group 5) or a control diet (group 6) for 62 weeks. Based on the results (not reported here), the study authors concluded that potassium chloride ingestion (as well as sodium chloride ingestion) demonstrated dose-dependent promoting effects, as evidenced by the number of atypical hyperplasias per rat, and a synergistic influence (potassium and sodium chloride), as evidenced by the number of adenocarcinomas during the post-initiation phase of two-stage glandular stomach carcinogenesis (Nishikawa et al., 1995). No no-observed-adverse-effect level (NOAEL) was determined.

The effects of neutral (KCl) and alkalizing ($KHCO_3$) salts on rat urinary bladder epithelium without prior exposure to a bladder tumour initiator was investigated. Male and female Wistar rats were supplemented with 3% KCl (approximately 1.5 g/kg bw per day), 4% $KHCO_3$ (approximately 2.0 g/kg bw per day), 2% $KHCO_3$ (approximately 1.0 g/kg bw per day) or a control diet for 78 or 130 weeks. The authors observed that, in the case of the potassium chloride-fed animals, the epithelial proliferations were associated with submucosal infiltrates or

overt cystitis, and that urine pH levels were unaffected. They concluded that, based on the results, potassium chloride was only a weak promotor (in the absence of an initiator), inducing only a few neoplastic lesions. The authors also observed that increased pH levels of urine resulting from the $KHCO_3$ treatment were necessary for urinary bladder cancer development (Lina et al., 1994). No NOAEL was determined.

The above studies indicate that potassium chloride is only a weak promotor of stomach and bladder cancers (in the absence of an initiator) and only at doses of potassium (1.25–2.5 g/kg bw per day) that far exceed those to which individuals would be exposed from drinking water or food.

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