Protective Effects of High Dietary Potassium: Nutritional and Metabolic Aspects

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ABSTRACT Potassium (K⁺) requirements have been largely overlooked because severe deficiencies are uncommon due to the ubiquity of this element in foods. However, a transition toward modern (“Westernized”) diets has led to a substantial decline of K⁺ intake compared with traditional food habits, and a large fraction of the population might now have suboptimal K⁺ intake. A high K⁺ intake was demonstrated to have protective effects against several pathologic states affecting the cardiovascular system, kidneys, and bones. Additionally, fruits and vegetables contain K/organic anion salts (malate, citrate), which exert alkalinizing effects, through KHCO₃ generation, which serves to neutralize fixed acidity in urine. Low-grade metabolic acidosis, when not properly controlled, may exacerbate various catabolic processes (bone Ca⁺ mobilization, proteolysis), especially in the elderly. Fruits and vegetables are therefore receiving great attention in a strategy to increase the nutritional value of meals while reducing energy density and intake. The need to ensure a 2.5- to 3.5-g daily K⁺ supply from fruits and vegetables represents a strong rationale for the “5–10 servings per day” recommendations. J. Nutr. 134: 2903–2906, 2004.

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In contrast to other major cations, potassium (K⁺) is rarely considered to be a critical dietary constituent whose supply should be optimized for better health. This relative lack of interest likely reflects the fact that K⁺ deficiencies of nutritional origin are uncommon because this element is quite ubiquitous, at least when diets are based on nonpurified foods. Nevertheless, due to the extensive use of processed foods, a significant fraction of the population in Westernized countries might suffer from a discrete but relevant K⁺ depletion, resulting in moderate chronic hypokalemia. Problems of excessive K⁺ availability are not a source of concern in healthy adults, except in subjects suffering terminal renal deficiencies or severe diabetes (1). Before the emergence of agriculture, and later of agroindustry, humans consumed a diet high in K⁺ (>200 mmol/d) and generally low in Na⁺. The recent increase in the consumption of processed foods, together with a reduction in fruit and vegetable consumption, has dramatically depressed K⁺ intake, in some cases falling below 50 mmol/d, in the presence of a large Na⁺ excess (1–3).

It is now well established that a high K⁺ intake plays a protective role against hypertension, stroke, cardiac dysfunctions, renal damage, hypercalciuria, kidney stones, and osteoporosis (4,5). In fact, optimization of dietary K⁺ is indicated not only in association with the above pathologic states, but also in connection with various other physiologic processes such as the acid-base status (6), and control of carbohydrate metabolism or energy balance.

Potassium in Foods. Potassium is the most abundant cation in eukaryotic cells (~140 mEq/L in the cytosol) and is thus amply supplied when intact or moderately altered tissues are consumed from plant (vegetables, legumes, or fruits) or animal foods (muscles or offal such as liver, heart, kidneys). In addition, some other foods such as milk (breast milk or cow’s milk: 50 or 160 mg/100 g, respectively) and cereals also contain significant amounts of K⁺.

This apparent ubiquity of K⁺ in foods should not obscure the following essential points: 1) the nutritional density (e.g., in mg K⁺/MJ) is generally lower in cereals and animal foods than in fruits and vegetables, with the exception of low-fat fishes; 2) refined fats or sugars are very low-K⁺ items, and their presence or addition in foods results in a lowering of K⁺ concentration as well as of nutritional density; 3) the accompanying anions for K⁺ are chiefly phosphate and chloride in animal products and cereals, whereas in fruits and vegetables, they are largely represented by organic anions such as citrate, malate, and to a lesser extent, oxalate or tartrate; 4) the K/organic anion ratio is lower than 0.5 in most fruits, whereas it always exceeds 1 in vegetables (up to 2.6 in pumpkins). Thus, even if lower than in fruits, the organic acidity of vegetables is more completely neutralized, giving them greater alkalinizing potency (7); 5) in contrast to Na⁺, Ca₂⁺, and Mg²⁺, most mineral waters are low in K⁺, and drinkable water is rarely a significant source of K⁺. Other beverages such as fruit juices, coffee, and tea, or liquid foods such as soups provide substantial quantities of K⁺; and 6) food processing often alters nutritional density; for example, highly refined wheat flour contains less than half of the K⁺ level of complete flour. Food processing such as boiling is probably a cause of K/organic salt losses, especially for vegetables because fruits are generally consumed uncooked. Steam cooking or brief frying are likely to maintain greater concentrations of K/malate or K/citrate than cooking procedures that lead to extensive leaching (Fig. 1).

Potassium in the Digestive Tract. Potassium salts are intrinsically very soluble and the conditions prevailing in the upper part of the digestive tract afford the release of the major
fraction of dietary K⁺ in the luminal water. The small intestine is the major site of K⁺ absorption (~90% of dietary K⁺). Because K⁺ is present in salivary, gastric, biliary, and pancreatic secretions, actual K⁺ absorption is higher than intake/output calculations might suggest. In the human small intestine, the cation permeability sequence is P₇ > P₈ > P₉, and, in all areas of the intestine, the rate of K⁺ absorption is highly dependent on luminal K⁺ concentration (8). Although it is not possible to exclude a component of active K⁺ transport, especially in the colon when dietary K⁺ intake is low, it is generally accepted that the dominant force for K⁺ absorption is passive diffusion. Presumably, passive diffusion occurs via the leaky tight junction pathway in the small intestine.

Fecal K⁺ excretion averages ~10 mEq/d when normal people ingest 90–100 mEq of dietary K⁺. When dietary K⁺ intake is increased, fecal K⁺ is scarcely altered, indicating that small intestinal absorption increases almost in direct proportion to increasing intake. Depending on the physiologic needs, K⁺ can be secreted in the colon via channels or reabsorbed by a luminal H⁺/K⁺-ATPase, which plays a critical role in the maintenance of K⁺ homeostasis during K⁺ deprivation (9). When dietary K⁺ is severely restricted, fecal K⁺ decreases to ~3.5 mEq/d, which presumably represents residual obligatory elimination. Humans eliminate ~80–100 g/d of bacteria, in which K⁺ is also the major intracellular cation (10); this could account for 6–8 mEq/d, hence the major part of fecal K⁺.

**Tissue Potassium Metabolism.** Extracellular K⁺ represents only ~2% of the total K⁺ body and this extracellular pool is of the same magnitude as K⁺ daily intake (70 mEq vs. 80–100 mEq/d). Some commonly consumed meals may provide >50 mEq K⁺ if they contain high-K⁺ plant foods (potatoes, various vegetables, fruits). Under such conditions, if there were no rapid and effective adjustment of renal excretion and/or transient tissue K⁺ storage, plasma K⁺ concentration might reach a critical level of 6–8 mEq/L, which would be potentially harmful for heart and nervous tissues. Furthermore, dietary K⁺ could pose a real challenge to body homeostatic systems for the following reasons: 1) the duodenum and the jejunum absorb K⁺ even more rapidly than water (8), and 2) renal excretion of K⁺ is progressive, especially when the body was previously adapted to low K⁺ meals (11). To match a massive K⁺ supply, several tissues have the capacity to transiently remove K⁺ from extracellular fluid, i.e., the muscles, in particular, and to a lesser extent the liver.

Rabinowitz et al. (12) proposed, in ruminants or rats, that K⁺ sensors in the gut, the portal circulation, and/or the liver could respond to local changes in K⁺ concentration. A hepatoportal bumetanide-sensitive Na⁺/K⁺-2Cl⁻ cotransporter (NKCC) could sense K⁺ concentration in the portal vein; when this mechanism is stimulated, kaliuresis would occur in response to activation of the periarterial hepatic nervous complex (13). Potassium uptake is also controlled by insulin, which circulates in portal blood at concentrations much higher than in peripheral blood. Nevertheless, the highest capacity to keep pace with a rapid rise in K⁺ absorption is clearly located in muscles. The muscle K⁺ pool is ~2700 mEq and the change in muscle K⁺ elicited by a 50 mEq load (a cantaloupe serving for example) would hardly exceed 2%, illustrating the considerable buffering capacities of muscles (14). However, the transfer of K⁺ into the muscle intracellular compartment takes place against a considerable concentration gradient and depends on active transport mediated by the Na⁺/K⁺-ATPase. This process is stimulated by hormones such as insulin (postprandial period) or catecholamines (after exercise, for example) (14). The uptake of K⁺ by Na⁺/K⁺-ATPase is intrinsically energy consuming, i.e., the transfer of 50 mEq K⁺ would require ~180 kcal (753 kJ)). The potential energy wastage of the transient K⁺ storage in muscle would be less if part of the K⁺ entered the intracellular compartment through other process(es). However, when K⁺ is absorbed together with glucose, the resulting insulin secretion was reported to stimulate the Na⁺/K⁺-ATPase (15) together with possibly inhibiting NKCC (non-ATP consuming process) activity (16).

A large fraction of filtered K⁺ is reabsorbed along the proximal tubule and the loop of Henle, whereas the late part of the distal tubule, the connecting tubule, and the cortical part of the collecting tubule are the major sites of K⁺ secretion. Factors promoting K⁺ secretion in the distal parts of the nephron include affluent K⁺ intake/aldosterone/tubular fluid flux, and alkalosis (17). On the other hand, shifting toward K⁺ reabsorption is essentially due to K⁺ losses and/or low-K⁺ diets. Exhaustive descriptions of the regulation of K⁺ renal transport were presented and they report a highly sophisticated control of ATP-dependent pumps and of various types of channels (18). With high-K⁺ diets, a large fraction of K⁺ excreted in the urine derives from secretion in the epithelial cells lining the late distal, connecting, and cortical collecting tubules. In these cells, apical mechanisms of K⁺ export involve passive movement of K⁺ along a favorable electrochemical gradient through selective ROMK channels (19). However, secretion of K⁺ depends ultimately on its active uptake.
by the Na\(^+/K^+\)-ATPase across the basolateral membrane. This is a potentially energy-consuming process, but it cannot compare with the tremendous work accomplished by the nephron to reabsorb 95–99% or the 25 mol of Na\(^+\) filtered each day (20).

**Potassium and Acid-Base Equilibrium.** Two common, often overlooked, conditions associated with chronic metabolic acidosis are aging and excessive protein ingestion. Even if the body's homeostatic response to these conditions is very efficient, homeostatic responses may engender pathologic consequences, such as nephrolithiasis, bone demineralization, and muscle protein breakdown (21). In this respect, K/organic salts that generate KHCO\(_3^-\) play an important role in neutralizing anions excreted in urine such as sulfate, an end-product of sulfur amino acid catabolism (22). Bicarbonate is not present in foods and may be produced within host tissues as a consequence of the oxidation of organic anions (essentially K\(^+\) malate or citrate salts). Malate and citrate, together with some minor others anions such as fumarate, succinate, or ketoglutarate, are effectively absorbed in the small intestine, probably through a Na-dicarboxylate cotransport (23). In contrast, oxalate or tartrate (present in spinach, rhubarb, or grapes) are poorly absorbed or metabolized. Enzymes metabolizing malate and citrate are ubiquitous and because these anions circulate in blood as trace amounts, it was assumed that they are essentially metabolized in the splanchnic area (intestine, liver) (7).

Potassium and organic anions, through KHCO\(_3^-\) generation or glutamine sparing, are very effective in neutralizing mineral acidity and favoring neutral or slightly alkaline urine pH (6). Alkalosis and K\(^+\) were also identified as major positive effectors of citrate excretion, with citrate considered to be a major crystallization inhibitor of calcium stone formation. Whether K\(^+\) directly affects the various processes activated by acidosis (citrate lyase, aconitase, Na-dicarboxylate cotransport) or merely operates by blunting acidosis remains unclear (24). In contrast, chronic K\(^+\) depletion inhibits renal brush border membrane Na/sulfate cotransport and leads to a reduction in serum sulfate levels (25). Thus, K\(^+\) plays a critical role in neutralizing excess sulfate ions (affluent sulfur amino acid provision, dietary sulfate) but also contributes to sulfate homeostasis through regulation of the expression of proximal tubular Na/sulfate-cotransporter.

**Potassium and Divalent Cation Homeostasis.** Calcium intake is frequently lower than nutritional recommendations in adults and the elderly, with adverse consequences on bone Ca\(^{2+}\) status and osteoporosis risk (26). Factors affecting the amounts of Ca\(^{2+}\) lost in urine, such as organic K\(^+\) salts, may be more effective than factors altering intestinal Ca\(^{2+}\) absorption. Thus, Appel et al. (27) observed a 30% decrease in urinary Ca\(^{2+}\) excretion when fruit and vegetable intake increased from 3.6 to 9.5 daily servings. Cell function, including that of osteoblasts, is normally impaired by acid; the stimulatory effect of acid on osteoblasts may represent a primitive "fail-safe" that evolved with terrestrial vertebrates to correct systemic acidosis by ensuring release of alkaline bone mineral when the lungs and kidneys are unable to remove sufficient H\(^+\) equivalent (28). Incubation in a reduced K\(^+\) medium stimulates Ca\(^{2+}\) efflux and osteoclastic enzyme release; it inhibits osteoblastic collagen synthesis, which may be mediated by a reduction in bone cell pH (29). In vivo, it is difficult to distinguish between specific K\(^+\) effects and alkalizing effects on bone resorption. From an epidemiologic point of view, Tucker et al. (30) reported that dietary components such as K\(^+\) contributed to the maintenance of bone density, and New (26) showed that fruit consumption was a predictor of greater bone density in postmenopausal women. It must be noted that concern about K\(^+\) intake is also relevant in younger subjects; in prepuberal children, Jones et al. (31) showed that urinary K\(^+\) correlated significantly with bone mass density at all skeletal sites (urinary K\(^+\) significantly correlated with K\(^+\) intake from fruit and vegetable). High salt intake is also a factor that can increase bone resorption in postmenopausal women, and high K\(^+\) intake ameliorates this adverse effect (32).

Magnesium is frequently provided by high-K\(^+\) foods because both cations represent major intracellular cations in eukaryotes. Although Mg\(^{2+}\) and K\(^+\) have distinct cellular roles, they may be subject to similar disturbances such as cell leakage, for example, in the case of metabolic acidosis. Inhibition of cardiovascular muscle Na\(^+/K^+\)-ATPase activity due to an increased level of the endogenous Na,K pump inhibitor (SPI) may be involved in the mechanism of volume expanded experimental and human essential hypertension (33). Furthermore, it was shown that high dietary K\(^+\)/Mg\(^{2+}\) have additive effects in preventing an increase in SPI, thus likely preventing a blood pressure increase (33). These data strongly suggest that various metabolic effects of K\(^+\) are modulated and/or amplified by Mg\(^{2+}\). This tight connection is illustrated in the study of Humphries et al. (2), which focused on a possible protective role of dietary Mg\(^{2+}\) in insulin resistance; their data also demonstrated a high degree of correlation of dietary K\(^+\) with insulin sensitivity. In fact, it was proposed that abnormalities in cellular ion homeostasis may be a major link between cardiovascular and metabolic diseases (34).

**Potassium and Glucose Tolerance.** It is well established that cellular uptake of K\(^+\) is tightly dependent on insulin, and that hyperglycemia is a potent stimulator of K\(^+\) uptake in normal subjects, with enhanced involvement of passive transfer processes (35). Short-term K\(^+\) deprivation leads to a nearly complete insulin resistance for cellular K\(^+\) uptake, preceding changes in muscle Na\(^+/K^+\)-ATPase expression (36). Insulin's actions on glucose uptake and K\(^+\) uptake are independently regulated by dietary fat and K\(^+\) content, respectively (37). Diabetes decreases the amount of Na\(^+/K^+\)-ATPase in skeletal muscles, heart, and nerves (38,39) and these changes may be important in the physiopathology of diabetes. K\(^+\) supplementation was shown to increase muscle Na\(^+/K^+\)-ATPase (improving extrarenal K\(^+\) homeostasis) (40), and dietary K\(^+\) could therefore play a preventive role against diabetes as illustrated by a prospective epidemiologic study of 84,360 U.S. women over 6 y showing that high K\(^+\) intake was associated with a lower risk of developing type 2 diabetes (41). At present, the effect of increasing K\(^+\) intake on the requirement for hypoglycemic drugs or insulin in diabetic patients is still poorly documented, even if K\(^+\) supplementation is clearly useful in patients with diabetic acidosis (1). In addition to insulin responsiveness, there is probably an association between the muscle Na\(^+/K^+\) ratio and energy expenditure in individuals genetically predisposed to the development of type 2 diabetes (39). On a larger scale, the DASH dietary pattern (increased intake of K\(^+\), Mg\(^{2+}\), and Ca\(^{2+}\)), which was included as part of an intervention for blood pressure control, enhanced insulin action beyond effects of an intervention that did not include DASH (42).

**Concluding Remarks.** As shown in this survey, an abundant K\(^+\) provision elicits a number of physiologic responses with recognized health consequences (1,4–6). Ensuring a daily K\(^+\)
supply of 2.5–3.5 g from fruits and vegetables (chiefly as citrate or malate) requires a daily intake of 0.6–0.8 kg, which is in line with the “5–10 servings per day” recommendations. Achieving higher daily intake of K\(^+\) would probably be beneficial, but this will require further efforts to achieve the following: 1) identification of the most effective sources of K\(^+\) in the diet; 2) optimizing food processing (especially for vegetables); 3) limiting the intake of empty calories; and 4) containing the cost of fruits and vegetables (a current WHO priority), major sources of K/organic anions.

**LITERATURE CITED**