

Potassium

Introduction

Potassium is an essential element required for a large number of physiological electrolyte and osmolar regulations (Oh and Uribarri 1999; Institute of Medicine [IOM] 2004). Potassium is widely available in food, and deficiency is more likely to be brought on by impaired renal function than by insufficient intake (McLaren 1999; IOM 2004). Manifestations of potassium deficiency include muscle weakness, respiratory inadequacy, hypotension, and electrocardiographic abnormalities. Similarly, potassium toxicity is more likely to result from renal insufficiency (due to decreased kidney function or decreased water intake) than from excess consumption (McLaren 1999).

Safety Considerations

Normal serum potassium levels are between 3.5 and 5.0 mEq per L. The risk of exceeding this level through normal dietary or supplemental intake of potassium is small in healthy adults. Cases of hyperkalemia (toxic levels of potassium in the blood, exceeding 6.5 mEq per L) are usually the result of renal failure or disorders such as Addison disease. Hyperkalemia can result in serious cardiac toxicity, but the amounts of potassium associated with such hyperkalemic states depend heavily on water consumption and kidney function. Because of the impact of these factors as well as that of other electrolytes (principally sodium and chloride), the evidence for potassium safety or toxicity at any particular intake level must be judged cautiously.

Several trials have evaluated the effects of potassium supplementation. Siani et al. (1991) found no adverse effects of potassium chloride at daily doses of 1,900 mg. Fotherby and Potter (1992) found no adverse effects at 2,340 mg per day. However, the evaluations for possible adverse effects (Expert Group on Vitamins and Minerals [EVM] 2003) were not specified endpoints in these clinical trials.

Potassium doses of 1,250 mg administered 3 times per day (for a daily total of 3,750 mg) produced only minor and infrequent adverse effects as revealed by endoscopy (McMahon et al. 1982). In a follow-up study, the wax-matrix formulation was administered in dosages ranging from 900 to 3,700 mg per day (McMahon et al. 1984). Endoscopically evident erosions of the upper GI tract were evident in a few subjects supplemented with 1,560 to 3,120 mg potassium per day for 21 months. Gastrointestinal symptoms were mild and did not correlate with lesions shown by endoscopic evaluation.

A meta-analysis of clinical trials on potassium (mostly potassium chloride) for possible lowering of blood pressure indicated that this mineral “appeared to be well tolerated in all studies included” (Whelton et al. 1997). The potassium dosages in those clinical trials ranged from 1,876 to 7,820 mg per day. The dietary potassium levels were not identified, but are usually in the 2 to 5 g range.

Official Reviews

Food and Drug Administration (FDA 1975). The FDA in 1975 issued a statement that “there have been several reports, published and unpublished, concerning nonspecific small-bowel lesions” related to use of oral drug products containing 100 mg or more potassium. It subsequently required precautionary labeling of such products. The FDA did not provide any dose-response evaluation that would justify such a finding, but concluded that any capsule or coated tablet of a potassium salt intended for oral ingestion without prior dilution with an adequate volume of liquid to preclude gastrointestinal injury should carry the FDA prescribed warning statement.

Expert Group on Vitamins and Minerals (EVM 2003). The UK’s EVM 2003 review concluded that the evidence was not sufficient to set an SUL for potassium but could support a guidance level. From the clinical trial evidence judged to be most relevant (McMahon et al. 1982; McMahon et al. 1984; Grimm et al. 1988, 1990), the EVM concluded that “supplemental doses of up to 3,700 mg potassium per day appear to be without overt adverse effects, but may be associated with gastrointestinal lesions diagnosed by endoscopy.” Based on this conclusion

(with no correction for uncertainty), the EVM set 3,700 mg per day as the guidance level. It was not specified whether this guidance level applied to supplemental potassium or total intake from all sources. The EVM recognized that the recommended nutrient intake (RNI) in the UK for potassium was 3,500 mg for adults over 18 years of age, but did not identify any estimate of average potassium intake by the population as a whole.

IOM (2004). The IOM has reviewed potassium, the other electrolytes, and water to establish new dietary reference intakes (DRIs). The IOM concluded that there was no evidence of chronic excess intakes of potassium in apparently healthy individuals and thus no UL was established.

European Food Safety Authority (EFSA 2005). EFSA concluded that the available data were insufficient to establish a UL for potassium, but noted that potassium intakes from foods in healthy individuals (average 3 to 4 g per day in adults, generally not exceeding 5 to 6 g per day), as well as supplemental potassium as potassium chloride of about 3 g per day, have not been associated with adverse effects. EFSA noted that certain groups are sensitive to increases in potassium intakes, in particular those with impaired renal excretion of potassium.

European Food Safety Authority (EFSA 2010). EFSA also published reviews of potassium and sodium sulfate safety in 2010. The EFSA Panel on Food Additives and Nutrient Sources Added to Food (ANS) was asked by the European Commission to deliver a scientific opinion on the safety of potassium sulfate and of sodium sulfate when added for nutritional purposes in food supplements as sources of, respectively, potassium and sodium. The review was limited to a review, per the petitioners' request, to review potassium sulfate used in food supplements to provide a maximum of 100 mg potassium per day for adults. EFSA concluded that the proposed use and use levels of potassium sulfate as a source of potassium were not a safety concern.

CRN Recommendations

The clinical trial data on potassium chloride, together with the epidemiology supporting the safety of larger amounts of potassium from fruits and vegetables, indicate that this nutrient has a wide margin of safety. Clinical trials collectively show no pattern of adverse effects for

supplemental potassium of 1,500 mg, with the potassium from food being unspecified. Larger quantities of potassium as potassium chloride can produce gastrointestinal effects, and these seem more likely if the daily total is ingested all at once, especially on an empty stomach. The EVM established a guidance level of 3,750 mg but did not distinguish between food intake and supplement intake. The evidence that was used in the EVM’s determination, however, related only to supplemental potassium.

Considering clinical trial evidence and the apparent safety of potassium intakes as high as 8 to 11 g per day from fruits and vegetables, CRN sets its ULS for potassium at 1,500 mg per day, with the provision that it should be divided into doses no larger than 500 mg each. There is no discernible scientific justification for the FDA threshold of 100 mg of potassium for regulation of products such as drugs that require a prescription caution statement.

Quantitative Summary for Potassium

CRN UL, supplemental intake	1,500 mg/day (500 mg, 3 times a day)
IOM UL, total intake	Not determined
EFSA UL, total intake	Not determined
EC supplement maximum	Not determined
EVM, guidance level, supplemental intake	3,700 mg/day

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