

Phosphorus

Introduction

Phosphorus in the phosphate form is an essential nutrient involved in many physiological processes, such as the body's energy cycle and regulation of acid-base balance. It is a component of cell membranes (as part of phospholipids); in cell regulation and signaling; and in the mineralization of bones and teeth (as part of hydroxyapatite). High-energy phosphate bonds are involved in the structure of the genetic materials DNA and RNA, and phosphorus helps the body make ATP, a molecule the body uses to store energy (Arnaud and Sanchez 1996; Knochel 1999).

The dietary requirement for phosphorus is based on the maintenance of normal serum phosphate levels in adults, which was also believed by the Institute of Medicine (IOM) to provide adequate intake to meet cellular and bone formation needs (IOM 1997). Phosphorus is widespread in the food supply, and dietary phosphorus deficiency is usually seen only in cases of anorexia or frank starvation. Phosphorus deficiency can result from the excessive use of antacids that contain aluminum hydroxide, which precipitates dietary phosphorus as insoluble and unabsorbable aluminum phosphate in the intestine (IOM 1997). While it is well established that phosphate and calcium are required for bone formation, emerging evidence suggests that phosphate supplementation may play a role in the effectiveness of calcium in reducing the risk of developing osteoporosis (Heaney and Nordin 2002; Heaney and Weaver 2003; Shapiro and Heaney 2003).

Safety Considerations

The phosphorus level in normal diets is not harmful, especially given adequate intakes of calcium and vitamin D (IOM 1997). Most dietary supplements do not contain significant amounts of phosphorus, and the contribution of dietary supplements to phosphorus intake is low (Bailey et al. 2011). A calcium-to-phosphorus ratio lower than 1 to 2 can cause small decreases in blood calcium levels; therefore, a ratio closer to 1 to 1 is considered superior. Phosphorus

requirements are influenced by interactions between calcium and phosphate, but studies have demonstrated that significant changes in phosphorous intake may not affect calcium balance in a meaningful way. For example, an increase in dietary phosphorus from 800 to 2,000 mg per day in adult males did not affect calcium balance regardless of calcium intake (Arnaud and Sanchez 1996).

In the absence of clinical signs of excess phosphorus, plasma phosphorus level is the most reliable indicator of excess phosphate (IOM 1997). There is no convincing scientific support for the widely accepted notion that consuming too much phosphorus from certain carbonated beverages contributes to calcium loss and increases the risk of osteoporosis (Heaney 2002). Indeed, the opposite effect may be true—calcium intake without simultaneous phosphorus intake may decrease the utilization of the calcium, at least partly neutralizing the potential benefits of the calcium on bone renewal.

Official Reviews

IOM (1997). The IOM reviewed dietary phosphorus for potential adverse effects, including adjustment in calcium-regulating hormones, metastatic calcification, skeletal porosity, and interference with calcium absorption, and found no evidence of any such activity (IOM 1997). In the absence of overt adverse effects, the IOM selected plasma phosphorus levels as the appropriate indicator of excess phosphorus intake. Therefore the IOM based its estimates of safe upper intake levels on the levels necessary to derange plasma phosphorus homeostasis. The IOM identified a NOAEL of 10.2 g per day and applied a UF of 2.5 to derive a UL of 4 g per day for adults. The UF of 2.5 is a default value meant to account for the uncertainty related to the pharmacokinetic relationship between food intake and blood levels (Petley et al. 1995). The IOM report indicates that phosphorus intakes may have increased dramatically over the last decade, thus creating concern about excessive phosphorus. This suggestion is counterbalanced by the evidence that calcium supplements can induce temporary low values in plasma phosphorus and that cosupplementation with calcium and phosphate can nullify this effect (Heaney 2002; Heaney and Nordin 2002).

Expert Group on Vitamins and Minerals (EVM 2003). The UK's EVM, like EFSA, found the existing evidence to be insufficient to derive an SUL value. It instead set a guidance level for total and supplemental phosphorus. The organization expressed concern about the few reports of mild gastrointestinal symptoms, such as osmotic diarrhea and gastrointestinal disturbance, reported in relation to supplemental phosphorus above 750 mg per day; on this basis it identified a NOAEL of 750 mg supplemental phosphorus per day. A guidance level of 250 mg supplemental phosphorus was identified by applying a default UF of 3 to this NOAEL. Assuming an intake of 2,100 mg from food and water, the EVM concluded that a guidance level of 2,400 mg was appropriate for phosphorus total intake from all sources.

European Food Safety Authority (EFSA 2006). In 2006 EFSA published its scientific opinion on the safe upper levels of phosphorous. The EFSA-appointed Scientific Panel on Dietetic Products, Nutrition and Allergies concluded that the available data are not sufficient to establish an upper level for phosphorus. The available data indicate that normal healthy individuals can tolerate phosphorus (phosphate) intakes up to at least 3,000 mg per day without adverse systemic effects. In some individuals, however, mild gastrointestinal symptoms have been reported if exposed to supplemental intakes above 750 mg phosphorus per day. There is no evidence of adverse effects associated with the current dietary intakes of phosphorus in EU countries.

CRN Recommendations

In adults with normal kidney function, phosphorus is readily excreted, and no imbalance in calcium metabolism occurs except at extreme intakes (Arnaud and Sanchez 1996). There are no data appropriate for identifying direct adverse effects of dietary phosphorus, and therefore no LOAEL can be identified. Similarly, no specific intake level qualifies as the NOAEL level. The very high NOAEL value identified by the IOM is perhaps too hypothetical, just as the very low NOAEL identified by the EVM was based on a speculative, worst-case interpretation of a very few reports of gastrointestinal side effects that could have had other causes. There is a need for an appropriate ratio of calcium-to-phosphorus intake within a broad range of acceptable ratios; therefore, in the absence of more specific evidence, a CRN UL of 1,500 mg is set for supplemental phosphorus.

Quantitative Summary for Phosphorus

CRN UL, supplemental intake	1,500 mg/day
IOM UL, total intake	4,000 mg/day
EFSA UL, total intake	Not determined
EC supplement maximum	Not determined
EVM, guidance level	250 mg/day supplement; 2,400 mg/day total intake

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