Published in final edited form as:
Adv Chronic Kidney Dis. 2013 March ; 20(2): 150–156. doi:10.1053/j.ackd.2012.10.008.

Sodium and phosphorus-based food additives: persistent but surmountable hurdles in the management of nutrition in chronic kidney disease

Orlando M. Gutiérrez, MD, MMSc
Division of Nephrology, Department of Medicine and Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL

Abstract

Sodium and phosphorus-based food additives are among the most commonly consumed nutrients in the world. This is because both have diverse applications in processed food manufacturing, leading to their widespread utilization by the food industry. Since most foods are naturally low in salt, sodium additives almost completely account for the excessive consumption of sodium throughout the world. Similarly, phosphorus additives represent a major and "hidden" phosphorus load in modern diets. These factors pose a major barrier to successfully lowering sodium or phosphorus intake in patients with chronic kidney disease. As such, any serious effort to reduce sodium or phosphorus consumption will require reductions in the use of these additives by the food industry. The current regulatory environment governing the use of food additives does not favor this goal, however, in large part because these additives have historically been classified as generally safe for public consumption. To overcome these barriers, coordinated efforts will be needed to demonstrate that high intakes of these additives are not safe for public consumption and as such, should be subject to greater regulatory scrutiny.

Keywords

nutrition; diet; sodium; phosphorus; chronic kidney disease

INTRODUCTION

Sodium-based food additives are among the most abundantly consumed nutrients in the world. This is because sodium salts are not only effective anti-spoilage agents, they can also serve as relatively cheap taste enhancers in a variety of foods. As a result, sodium additives are heavily utilized in processed foods, accounting for the vast majority of the excess sodium consumed throughout the world. Though discovered and utilized as a food additive later than sodium, phosphorus-based food additives have taken on a similar wide berth of uses, including as food preservatives and taste enhancers. Like sodium, phosphorus additives have become nearly indispensable in food manufacturing, substantially

Corresponding author: Orlando M. Gutiérrez, MD, MMSc, University of Alabama at Birmingham, ZRB 614, 1720 2nd AVE S., Birmingham, AL, 35294-0006 phone: 205-996-2736 fax: 205-996-6465, ogutierr@uab.edu.

Financial disclosures: None

augmenting the phosphorus content of processed foods. The public health consequences of these trends have been well-publicized, particularly with respect to the link between excess dietary sodium intake and the increasing prevalence and severity of hypertension in both the developed and developing world. These trends have more ominous implications for millions of individuals living with chronic kidney disease (CKD), who have reduced capacity to excrete even normal dietary sodium and phosphorus loads. This review will focus on the impact of sodium- and phosphorus-based food additives on total daily intake of sodium and phosphorus in contemporary diets, the special implications this may have for individuals with chronic kidney disease, and potential strategies for reducing the consumption of sodium and phosphorus-based food additives in CKD patients.

Sodium Additives

Sodium-based food additives were introduced into the human diet somewhere between 5,000 to 10,000 years ago when they were found to retard the spoilage of poultry and meat products.[1] This discovery revolutionized the capacity for early societies to preserve meat for personal consumption and/or trade purposes, markedly increasing the use of sodium in a variety of foodstuffs. The importance of this discovery is evident from historical records which show that access to salt was a cherished commodity in early societies, on par with the finest measures of wealth and social standing, and in some cases, used as a form of currency.[1, 2]

Historically, the primary reason to add sodium to foods was as a method for food preservation,[1] based largely upon sodium's antimicrobial properties.[3] With the advent of refrigeration and other advances in food preservation, the primary motivations evolved beyond just anti-spoilage agents to enhancing the taste and palatability of foods.[4] Salt (hereby referring to sodium chloride) has a number of desirable effects on foodstuffs, including improving the intensity of flavor and augmenting the overall perception of product thickness and fullness.[5, 6] Consistent with this, there is remarkable congruity with respect to the excessive levels of sodium consumption across countries with very different culinary traditions,[7, 8] suggesting a strong salt preference in human populations.[9] Along with its preservative and taste-enhancing effects, salt is also commonly used in the fermentation, emulsification, leavening, and enhancement of foods,[10] contributing to very high levels of salt usage by the food manufacturing industry.

Since most food items contain relatively low amounts of sodium naturally, the introduction of sodium additives into human food supplies effectively increased the average daily consumption of sodium from less than 400 mg per day in pre-historic times to an average of 4,000 mg per day in modern times, far above current recommendations for daily intake (**Table 1**).[8, 11] It is estimated that only 10% of daily salt intake in Western populations comes from natural sources, whereas 75% comes from salt added to processed foods by manufacturers, and the remaining 15% from salt added during cooking or other discretionary uses.[12] While Asian populations manifest similarly high levels of added sodium intake,[8] there is important variability in the sources of added sodium in Eastern vs. Western countries. This was perhaps best demonstrated in the INTERMAP study, a large international cooperative study that estimated the quantity and sources of sodium intake in 4,680 individuals 40 to 59 years of age from Japan, the People's Republic of China, the United Kingdom and the United States.[13] This study showed that the majority of sodium intake in the United Kingdom and the United States came from processed breads, cereals, grains, meats, sauces and canned items with only a very small fraction (5 - 10%) coming from salt added in home cooking or at the table.[8] In contrast, the majority of salt intake in Japan came from soy sauce, salted fruits and vegetables, miso soup, and fish, whereas in China, the vast majority of sodium intake (76%) came from salt added during home cooking

or at the table. These differences highlight the importance of regional factors in determining the sources of sodium intake in the developed and developing world.

Health Impact of Sodium Additives in Individuals with Chronic Kidney Disease—Large observational studies have shown that excess salt intake is associated with adverse health outcomes among individuals with normal kidney function, including hypertension, cardiovascular disease events and excess urinary albumin excretion.[14-17] Randomized trials have largely corroborated these relationships,[18-20] most notably the Dietary Approaches to Stop Hypertension (DASH)-Sodium Collaborative Research Group that showed that diets low in sodium significantly reduced blood pressure in study participants.[21] These findings are in line with animal data showing that excess dietary sodium intake increases systemic blood pressure, induces left ventricular hypertrophy and promotes vascular damage.[15, 22]

The adverse effects of excess dietary sodium intake are magnified in individuals with CKD. Much like individuals with normal kidney function who are classified as "salt sensitive,"[23] individuals with CKD have impaired neurohormonal mechanisms for enhancing excess sodium excretion in the urine, resulting in maladaptive increases in systemic blood pressure, renal plasma flow, and ultimately glomerular filtration pressure.[24, 25] All of these factors, in turn, strongly contribute to the development of hypertension, vascular injury, and their sequelae including proteinuria and progression of renal failure, in CKD patients.[2, 26] Since sodium additives make up the lion's share of excess sodium consumption in the food supply, reducing the intake of sodium additives is paramount to improving cardiovascular and renal outcomes in CKD patients consuming a typical Westernized diet.

Regulation of Sodium Additive Use—Since only a small fraction of sodium consumed on a daily basis comes from discretionary sodium use (with the notable exception of the People's Republic of China), sodium additives in processed foods represent the single greatest barrier to lowering sodium intake in CKD patients, particularly those who do not have the financial means to purchase fresh foods. As such, any serious public health efforts to reduce the intake of sodium in CKD patients will have to include a strategy for reducing the use of sodium additives by the food manufacturing industry.

In order to understand the key regulatory barriers to attaining this goal in the US, it is helpful to review some of the legal framework underlying food additive regulation. Much of the framework is based upon the 1958 Food Additives Amendment (FAA) to the Federal Food, Drug, and Cosmetic Act of 1938.[27] In brief, this amendment defined any substances intentionally added to food by manufacturers as "food additives," and required manufacturers to obtain approval from the Food and Drug Administration (FDA) prior to adding these substances to food (it should be noted at this juncture that the legal definition of a "food additive" as established by the FAA differs quite a bit from the more colloquial uses of the term—for this reason, food additives will be put in parentheses when referring to the legal sense of the term here on out). This approval included the requirement that substances meet the relatively steep safety standard of "reasonable certainty of no harm" under the conditions of its intended use. Importantly, however, substances that were used in ways generally recognized as safe (GRAS) or that were used in ways previously sanctioned by the FDA or the Department of Agriculture prior to the enactment of the FAA were excluded from this definition. This is critical in that most uses of salt at that time (and continuing through today) were able to be excluded from the definition of a "food additive" under these provisions, exempting salt and other sodium-based ingredients from undergoing the stringent pre-market reviews of safety required for "food additives" by the FAA.

Recognizing the importance of reviewing the GRAS status of substances over time, the FDA in 1969 designated a Select Committee on GRAS Substances (SCOGS) to review the safety

profile of all current GRAS substances (including salt).[10] The findings of this report raised substantive concerns about whether salt met the "reasonable certainty of no harm" safety standard, which could put it status as a GRAS substance in peril and thus, subject it to greater regulation. However, the FDA did not modify the status of salt after reviewing the results of the report, saying in essence that it did not have enough evidence to overturn its GRAS status.[10] There have been further attempts to reduce salt intake over the past 32 years, including a publication of a "Policy Notice" in 1982 in which the FDA called for a reduction in salt in processed foods through public education, voluntary industry efforts, and expanded disclosure of sodium content on product labels.[10] More recently, the FDA has proposed to mandate the listing of sodium content of foods in fast food establishments and restaurants in order to make it easier for consumers to identify lower sodium options.[10] In addition, a 2010 Institute of Medicine report detailed a number of strategies to gradually reduce sodium content of processed foods over time.[10] To date, however, these efforts have led to only marginal reductions in sodium additive intake in the US.[28]

Phosphorus Additives

Dietary phosphorus consists of both "organic" sources of esterified phosphorus, such as meats, dairy products and vegetables, and "inorganic" forms of phosphorus that are commonly added to processed foods and beverages.[29-31] Unlike sodium, organic or natural forms of phosphorus are plentiful in the food supply, making up the majority of phosphorus consumed on a daily basis.[32] However, phosphorus-based additive use exploded during the 20th century,[33] substantially augmenting total phosphorus intake in modern diets.

Phosphorus-based additives serve a number of critical functions for food manufacturing, including pH stabilization, metal cation sequestration, emulsification, leavening, hydration, and bactericidal actions, among others.[33] Because of this wide diversity of applications, the use of phosphorus additives in the food manufacturing industry is immense—for example, over 40 million pounds of phosphorus additives were used annually in the US during the 1970's by the meat industry alone,[33] a figure that has likely grown over the past 40 years as demand for convenience and fast foods has increased. The magnitude of the use of phosphorus additives in the meat industry pales in comparison to that of the baking industry, which utilizes the highest quantities of phosphorus additives because of the key role that phosphorus acids play as dough leavening agents.[34] In a report commissioned by the U.S. Department of Commerce in 1972, baked goods were estimated to contain nearly 10-fold higher amounts of phosphorus additives than meat products.[35] Phosphorus additives, including those complexed with sodium, are also commonly used in milk and dairy products (particularly processed cheeses), seafood, and beverages. Dark colas and sodas in particular are the beverages that contain the highest amounts of phosphorus additives, principally in the form of phosphoric acid.[36]

Most individuals in the U.S. easily receive—and in fact usually exceed—the recommended daily allowance (RDA) of dietary phosphorus. Although the current RDA for phosphorus is 700 mg per day for adults (Table 1),[37] the most recent estimates of average daily intake for US adults 20 years of age and older is ~1550 mg for males and ~1120 mg for females, due in large part to the high intake of phosphorus-rich foods in the American diet.[38] The nearly ubiquitous distribution of phosphorus additives in processed foods augments phosphorus intake even further,[39] with estimates ranging from 250 to 1,000 mg of extra phosphorus per day.[40-42] should be noted, however, that some of the studies from which these estimates were derived have important limitations. For example, in one highly-cited study, healthy volunteers were fed a balanced diet consisting of additive-free food for four weeks, after which they were fed a diet that looked virtually identical with the only difference being that instead of being additive-free, the foods were additive-rich.[40] The measured content of phosphorus in the additive-rich diet was approximately 1,000 mg higher per day than in the

additive-free diet, suggesting that additive-enhanced foods can nearly double total phosphorus intake per day. However, the meat products used as additive-rich foods in this study were manufactured using quantities of phosphorus additives nearly twice that normally used by the meat industry,[33] likely exaggerating the difference in phosphorus content between the diets. Furthermore, the study was specifically designed to accentuate the differences between an additive-free and an additive-rich diet, and thus, may not be representative of more real-world scenarios in which individuals are consuming a mixture of both. Nevertheless, irrespective of the exact quantity, studies have shown that phosphorus additives can substantially increase phosphorus contents of processed foods.[29, 32, 43]

Importantly, despite their widespread use, phosphorus additives are typically unaccounted in the estimated phosphorus content of processed foods because food manufacturers are not required to list their quantities.[31] Thus, not only do phosphorus additives increase daily phosphorus intake, they represent a largely "hidden" dietary phosphorus load in typical American diets. This is noteworthy in that phosphorus additives are absorbed with much greater efficiency in the gut (> 90%) than organic forms of phosphorus in animal or vegetable proteins (~50-60%), with potentially important consequences.[31] Indeed, a study showed that foods with higher phosphorus bioavailability significantly increased serum phosphate and fibroblast growth factor 23 (FGF23) concentrations in CKD patients,[44] suggesting that the high bioavailability of phosphorus additives may potentiate their adverse impact on phosphorus homeostasis in CKD.

Health Impact of Phosphorus Additive Use in CKD patients—Unlike sodium, data on the health impact of phosphorus additives are sparse in the general population, and nearly non-existent in individuals with kidney disease. Although a number of studies have examined the adverse effects of oral phosphate supplement loading in healthy volunteers,[45-47] supplement loading does not take into account the effects of food processing or cooking on the biochemical properties of food additives, making it unclear how well these studies captured the physiological effects of commercial food additives in humans. The few studies that did examine the effects of additives found in commercially-processed foods were primarily done in healthy female volunteers, and in general showed that high phosphorus additive intake promoted bone loss, partly though disruptions in calcium balance.[48-54] Whether high phosphorus additive intake has adverse effects on blood pressure or kidney function in healthy individuals has not been studied in detail and should be the focus of future investigation.

To date, no physiological studies have specifically examined the impact of commercially-derived phosphorus additives on bone and mineral metabolism in individuals with CKD. However, one study did examine the impact of lowering phosphorus additive intake on serum phosphate concentrations in hemodialysis patients. In this study, maintenance hemodialysis patients were taught how to read product labeling while grocery shopping in order to avoid purchasing items containing phosphorus additives and how to make better choices in choosing low-phosphorus options when eating at local fast food restaurants.[55] After three months of the intervention, mean serum phosphate concentrations declined by 1.0 mg/dl in patients who received the intervention as compared to 0.4 mg/dl in control patients who did not (*P* for difference 0.02), suggesting a modest benefit of avoidance of phosphorus additives in hemodialysis patients. The extent to which avoidance of phosphorus additives improves phosphorus homeostasis in pre-dialysis CKD patients consuming typical Westernized diets is unclear and should be the focus of future studies.

Regulation of Phosphorus Additive Use—In recognition of the already high intake of natural forms of phosphorus in modern diets, several regulatory agencies—most notably the Joint Food and Agriculture Organization /World Health Organization Expert Committee on

Food Additives (JEFCA) and the aforementioned SCOGS from the FDA—commissioned separate studies to assess the safety of phosphorus additives in processed foods. The JEFCA report, released in 1964, evaluated all available studies examining acute and chronic toxicities of high phosphorus intake.[56] The main findings of the report were that phosphorus compounds commonly used as food additives at that time appeared to be safe for public consumption as long as they were not ingested in excess amounts. To aid in determining what would constitute excess amounts, the committee recommended upper limits of daily phosphorus additive intake deemed to be safe for healthy populations. Two thresholds were recommended—an "unconditional zone of acceptability" and a "conditional zone of acceptability." The unconditional zone (30 mg/kg a day or 2,100 mg/day in a 70 kg person) represented the level of phosphorus additive use that was deemed effective for the intended purpose of the additive and could "be safely employed without further expert advice," for example from a panel of nutrition specialists.[57] The conditional zone (30 to 70 mg/kg day) represented levels that could be used safely in the community, but which should have some level of expert supervision that could be readily available for direction or advice.

Like the JEFCA report, the 1975 SCOGS report reviewed many of the same studies from the 1950's through the early 1970's, and came to the conclusion that phosphorus-based food additives posed little threat to consumer safety when used in quantities that "are now current or might reasonably be expected in the future."[58] As such, the FDA kept phosphorus additives among the group of GRAS substances, saying in summary, that "None of the GRAS phosphates is intrinsically harmful and their use in foods does not present a hazard when the total amount of phosphorus ingested and the intakes of calcium, magnesium, vitamin D and other nutrients are satisfactory."[58]

While it is possible that phosphorus additives are safe for public consumption when used under these conditions, critical limitations in the literature used to derive these recommendations should prompt caution before drawing this conclusion. First, the vast majority of animal studies cited by these reports were conducted in the 1960's and 1970's, 20 – 30 years before the biological basis for a direct link between excess phosphorus and cardiovascular disease (ie, vascular calcification) was first reported.[59] As a result, while renal and bone toxicities were carefully evaluated in these studies, the impact of excess phosphorus intake on cardiovascular health was examined in much less detail. Moreover, critical hormones involved in phosphorus homeostasis, most notably FGF23, were unknown in that era. FGF23 is a novel phosphaturic hormone that is stimulated by increased dietary phosphorus intake.[60] High FGF23 concentrations have been strongly associated with cardiovascular disease, including vascular calcification, endothelial dysfunction and left ventricular hypertrophy.[61-64] Since FGF23 was not discovered until the beginning of this century,[65] none of these older studies examined the potential adverse effects of phosphorus additives on FGF23 secretion. Finally, very few of these studies were conducted in humans. This is a critical gap in the literature given that phosphorus toxicology research in animals rarely accounts for food processing conditions such as cooking, which may modify the biochemical properties of food additives.[33] For all these reasons, the full public health implications of the high use of phosphorus additives in the food manufacturing industry remain largely unknown.

Sodium and Phosphorus-based Food Additives: Assessing the Forks in the Road

As the above discussion makes clear, addressing the high use of the additives in processed foods is critical for meaningfully reducing sodium and phosphorus intake in the general population, and CKD patients in particular, since these foods constitute such a large proportion of what most individuals consume. Although a comprehensive review of all the steps needed to arrive at this objective is beyond the scope of this review, several key points will be emphasized below.

First, any federally-mandated reductions in sodium will likely require either revoking sodium's GRAS status (i.e., re-classifying it as a "food additive"), or altering sodium's GRAS status to require more stringent safety standards, including limitations in the quantities that can be added to food. Both maneuvers would likely hinge on being able to convince the FDA (and other powerful political interests) that sodium-based additives violate the "reasonable certainty of no harm" safety standard, and as such, require greater monitoring and regulation. Unfortunately, this is not straight-forward, as there are a number of practical and legal hurdles that would need to be overcome to accomplish this goal (reviewed in-depth in reference [10]). Nevertheless, the large and growing body of evidence showing that high sodium intake poses a real and present public health danger would form a strong foundation for sustaining such an effort. The same cannot be said about phosphorus-based food additives. Indeed, as mentioned above, data on the impact of phosphorus additives in humans is limited and/or largely extrapolated from animal studies over forty years old. Therefore, before the safety of phosphorus additives can be reasonably challenged, more studies are needed to determine the full impact of these additives on mineral metabolism and cardiovascular health.

Second, any efforts to reduce sodium additives in processed foods, whether by federal mandate or public education programs, will likely fail without addressing the strong salt preference in human populations. Indeed, the single greatest barrier to the voluntary reduction in the use of sodium additives by the food industry has been the well-founded fear that doing so would drive consumers to higher-sodium-containing products made by competitors.[10] Because of this, any sustainable reductions in sodium additive use will likely require slow, step-wise, and across-the-board decreases in sodium content so that consumers gradually become accustomed to lower sodium intake, with no manufacturer gaining a competitive edge over another. Whether similar issues apply to phosphorus additives is less clear. However, given phosphorus additives' diversity of applications in improving the taste, appearance, and shelf-life of foods, it is very possible that consumer preferences could also curtail efforts to reduce their use if these additives were lowered in too rapid or uncoordinated a manner.

Third, it will be quite important to mind the "law of unintentional consequences" in the process of implementing any of these initiatives. Indeed, it is quite ironic that previous attempts to reduce the content of sodium in food additives may have inadvertently increased the use of phosphorus additives. As postulated by one authority in the field of phosphorus additives, interest in the use of these additives in meat products spiked in the 1980's in response to several position papers from the US National Academy of Sciences calling for reductions in the use of sodium as food additives.[33] This is because phosphorus can replace many of the functions of sodium in food processing, making phosphorus additives natural alternatives to sodium, and potentially accounting for the increase in the use of these additives in the US over the past 30 years.[50] As another sobering example, efforts to reduce salt added to ready-to-eat foods in the United Kingdom were linked to an outbreak of listeriosis from 2001 to 2005.[10] Given sodium's strong anti-microbial actions against pathogens such as *Clostridium botulinum* and *Listeria monocytogenes*, it will be important to understand the safety implications of reducing sodium or phosphorus in processed foods before additive-lowering programs are widely adopted.

Though formidable, none of these barriers are insurmountable. As any sustainable in-roads in reducing sodium and phosphorus intake in modern diets will require a coordinated action at all levels, it is hoped that by having a better understanding of the scope of the issue, how it uniquely impacts CKD patients, and the major impediments in resolving the situation, the nephrology community can better focus its energy and efforts in successfully working with industry, the government, and, most importantly, patients, to achieve these goals. Given that

nutrition plays such a key role in CKD outcomes, these issues should be among the highest priorities in the research and clinical community.

Acknowledgments

Dr. Gutiérrez was supported by grants K23DK081673 and R03DK095005.

REFERENCES

1. Macgregor, G.; de Wardener, HE. Salt, diet and health: Neptune's poisoned chalice: the origins of high blood pressure. Cambridge University Press; Cambridge, UK: 1998.
2. Ritz E. Salt--friend or foe? Nephrol Dial Transplant. 2006; 21(8):2052–2056. [PubMed: 16384834]
3. Shelef, LA.; Seiter, J. Indirect and miscellaneous antimicrobials. In: Davidson, PM.; Sofos, JN.; Larry, BA., editors. Antimicrobials in food. 3rd ed. Taylor and Francis; Boca Raton, FL: 2005. p. 573-598.
4. He, FJ.; Macgregor, GA. Dietary salt, high blood pressure and other harmful effects on health. In: Kilcast, D.; Angus, F., editors. Reducing salt in foods: Practical strategies. Woodhead; Cambridge, UK: 2007. p. 18-54.
5. Breslin PA, Beauchamp GK. Salt enhances flavour by suppressing bitterness. Nature. 1997; 387(6633):563. [PubMed: 9177340]
6. Gillette M. Flavor effects of sodium chloride. Food Technology. 1985; 39(6):47–52.
7. Intersalt Cooperative Research Group. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. BMJ. 1988; 297(6644):319–328. [PubMed: 3416162]
8. Anderson CA, Appel LJ, Okuda N, et al. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc. 2010; 110(5):736–745. [PubMed: 20430135]
9. Mattes RD. The taste for salt in humans. Am J Clin Nutr. 1997; 65(2 Suppl):692S–697S. [PubMed: 9022567]
10. Committee on Strategies to Reduce Sodium Intake. Strategies to Reduce Sodium Intake in the United States. Institute of Medicine, The National Academies Press; Washington, D.C.: 2010.
11. Blackburn H, Prineas R. Diet and hypertension: anthropology, epidemiology, and public health implications. Prog Biochem Pharmacol. 1983; 19:31–79. [PubMed: 6338525]
12. James WP, Ralph A, Sanchez-Castillo CP. The dominance of salt in manufactured food in the sodium intake of affluent societies. Lancet. 1987; 1(8530):426–429. [PubMed: 2880223]
13. Stamler J, Elliott P, Dennis B, et al. INTERMAP: background, aims, design, methods, and descriptive statistics (nondietary). J Hum Hypertens. 2003; 17(9):591–608. [PubMed: 13679950]
14. He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. J Hum Hypertens. 2009; 23(6):363–384. [PubMed: 19110538]
15. Meneton P, Jeunemaitre X, de Wardener HE, MacGregor GA. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev. 2005; 85(2):679–715. [PubMed: 15788708]
16. Aaron KJ, Campbell RC, Judd SE, Sanders PW, Muntner P. Association of dietary sodium and potassium intakes with albuminuria in normal-weight, overweight, and obese participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Am J Clin Nutr. 2011; 94(4):1071–1078. [PubMed: 21880845]
17. Forman JP, Scheven L, de Jong PE, Bakker SJ, Curhan GC, Gansevoort RT. Association between sodium intake and change in uric acid, urine albumin excretion, and the risk of developing hypertension. Circulation. 2012; 125(25):3108–3116. [PubMed: 22711274]
18. Cook NR, Cutler JA, Obarzanek E, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ. 2007; 334(7599):885–888. [PubMed: 17449506]

19. He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens. 2002; 16(11):761–770. [PubMed: 12444537]
20. Forte JG, Miguel JM, Miguel MJ, de Padua F, Rose G. Salt and blood pressure: a community trial. J Hum Hypertens. 1989; 3(3):179–184. [PubMed: 2671369]
21. Sacks FM, Svetkey LP, Vollmer WM, et al. DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. N Engl J Med. 2001; 344(1):3–10. [PubMed: 11136953]
22. Sanders PW. Vascular consequences of dietary salt intake. Am J Physiol Renal Physiol. 2009; 297(2):F237–243. [PubMed: 19339634]
23. Roos JC, Koomans HA, Dorhout Mees EJ, Delawi IM. Renal sodium handling in normal humans subjected to low, normal, and extremely high sodium supplies. Am J Physiol. 1985; 249(6 Pt 2):F941–947. [PubMed: 3907374]
24. Cianciaruso B, Bellizzi V, Minutolo R, et al. Renal adaptation to dietary sodium restriction in moderate renal failure resulting from chronic glomerular disease. J Am Soc Nephrol. 1996; 7(2): 306–313. [PubMed: 8785401]
25. Koomans HA, Roos JC, Dorhout Mees EJ, Delawi IM. Sodium balance in renal failure. A comparison of patients with normal subjects under extremes of sodium intake. Hypertension. 1985; 7(5):714–721. [PubMed: 3897045]
26. Krikken JA, Laverman GD, Navis G. Benefits of dietary sodium restriction in the management of chronic kidney disease. Curr Opin Nephrol Hypertens. 2009; 18(6):531–538. [PubMed: 19713840]
27. Food Additives Amendment of 1958. Public Law 85-929; 72 Stat 1784.
28. Bernstein AM, Willett WC. Trends in 24-h urinary sodium excretion in the United States, 1957-2003: a systematic review. Am J Clin Nutr. 2010; 92(5):1172–1180. [PubMed: 20826631]
29. Sherman RA, Mehta O. Phosphorus and potassium content of enhanced meat and poultry products: implications for patients who receive dialysis. Clin J Am Soc Nephrol. 2009; 4(8):1370–1373. [PubMed: 19628683]
30. Sherman RA, Mehta O. Dietary phosphorus restriction in dialysis patients: potential impact of processed meat, poultry, and fish products as protein sources. Am J Kidney Dis. 2009; 54(1):18–23. [PubMed: 19376617]
31. Uribarri J, Calvo MS. Hidden sources of phosphorus in the typical American diet: does it matter in nephrology? Semin Dial. 2003; 16(3):186–188. [PubMed: 12753675]
32. Uribarri J. Phosphorus additives in food and their effect in dialysis patients. Clin J Am Soc Nephrol. 2009; 4(8):1290–1292. [PubMed: 19608709]
33. Molins, RA. Phosphates in Food. CRC Press, Inc.; Boca Raton: 1991.
34. Stahl, JL.; Ellinger, RH. In: Deman, JM.; Melnychyn, P., editors. The use of phosphate in the cereal and baking industry; Symposium: Phosphate in Food Processing; Westport, CT: The Avi Publishing Company, Inc.. 1971; p. 194-212.
35. GRAS (Generally Recognized as Safe). Food Ingredients-- Phosphates. The Franklin Institute Research Labs; Philadelphia, PA: 1972.
36. Murphy-Gutekunst L. Hidden phosphorus in popular beverages. Nephrol Nurs J. 2005; 32(4):443–445. [PubMed: 16180787]
37. Dietary Reference Intakes for Calcium. Phosphorus, Magnesium, Vitamin D, and Fluoride. The National Academies Press; 1997.
38. US Department of Agriculture ARS. Nutrient Intakes from Food: Mean Amounts Consumer per Individual, by Race/Ethnicity and Age2010. Available: www.ars.usda.gov/ba/bhnrc/fsrg
39. Uribarri J. Phosphorus homeostasis in normal health and in chronic kidney disease patients with special emphasis on dietary phosphorus intake. Semin Dial. 2007; 20(4):295–301. [PubMed: 17635818]
40. Bell RR, Draper HH, Tzeng DY, Shin HK, Schmidt GR. Physiological responses of human adults to foods containing phosphate additives. J Nutr. 1977; 107(1):42–50. [PubMed: 189000]
41. Calvo MS. Dietary considerations to prevent loss of bone and renal function. Nutrition. 2000; 16(7-8):564–566. [PubMed: 10906557]

42. Oenning LL, Vogel J, Calvo MS. Accuracy of methods estimating calcium and phosphorus intake in daily diets. J Am Diet Assoc. 1988; 88(9):1076–1080. [PubMed: 3418003]
43. Benini O, D'Alessandro C, Gianfaldoni D, Cupisti A. Extra-phosphate load from food additives in commonly eaten foods: a real and insidious danger for renal patients. J Ren Nutr. 2011; 21(4): 303–308. [PubMed: 21055967]
44. Moe SM, Zidehsarai MP, Chambers MA, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. Clin J Am Soc Nephrol. 2011; 6(2): 257–264. [PubMed: 21183586]
45. Antoniucci DM, Yamashita T, Portale AA. Dietary phosphorus regulates serum fibroblast growth factor-23 concentrations in healthy men. J Clin Endocrinol Metab. 2006; 91(8):3144–3149. [PubMed: 16735491]
46. Burnett SM, Gunawardene SC, Bringhurst FR, Juppner H, Lee H, Finkelstein JS. Regulation of C-terminal and intact FGF-23 by dietary phosphate in men and women. J Bone Miner Res. 2006; 21(8):1187–1196. [PubMed: 16869716]
47. Ferrari SL, Bonjour JP, Rizzoli R. Fibroblast growth factor-23 relationship to dietary phosphate and renal phosphate handling in healthy young men. J Clin Endocrinol Metab. 2005; 90(3):1519–1524. [PubMed: 15613425]
48. Calvo MS, Kumar R, Heath H 3rd. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. J Clin Endocrinol Metab. 1988; 66(4):823–829. [PubMed: 2831248]
49. Calvo MS, Kumar R, Heath H. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. J Clin Endocrinol Metab. 1990; 70(5):1334–1340. [PubMed: 2335575]
50. Calvo MS, Park YK. Changing phosphorus content of the U.S. diet: potential for adverse effects on bone. J Nutr. 1996; 126(4 Suppl):1168S–1180S. [PubMed: 8642452]
51. Karkkainen M, Lamberg-Allardt C. An acute intake of phosphate increases parathyroid hormone secretion and inhibits bone formation in young women. J Bone Miner Res. 1996; 11(12):1905–1912. [PubMed: 8970892]
52. Karp HJ, Vaihia KP, Karkkainen MU, Niemisto MJ, Lamberg-Allardt CJ. Acute effects of different phosphorus sources on calcium and bone metabolism in young women: a whole-foods approach. Calcif Tissue Int. 2007; 80(4):251–258. [PubMed: 17401693]
53. Kemi VE, Karkkainen MU, Lamberg-Allardt CJ. High phosphorus intakes acutely and negatively affect Ca and bone metabolism in a dose-dependent manner in healthy young females. Br J Nutr. 2006; 96(3):545–552. [PubMed: 16925861]
54. Kemi VE, Rita HJ, Karkkainen MU, et al. Habitual high phosphorus intakes and foods with phosphate additives negatively affect serum parathyroid hormone concentration: a cross-sectional study on healthy premenopausal women. Public Health Nutr. 2009; 12(10):1885–1892. [PubMed: 19216809]
55. Sullivan C, Sayre SS, Leon JB, et al. Effect of food additives on hyperphosphatemia among patients with end-stage renal disease: a randomized controlled trial. JAMA. 2009; 301(6):629–635. [PubMed: 19211470]
56. Joint FAO/WHO Expert Committee on Food Additives. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation: Emulsifiers, Stabilizers, Bleaching and Maturing Agents. World Health Organization; Geneva: 1964.
57. Food and Agriculture Organization. Evaluation of a number of anti-microbials and antioxidants. FAO Nutrition Meeting Report. Rome1961B.
58. Food and Drug Administration. Evaluation of the health aspects of phosphate as food ingredients. 1975 NTIS PB-262-65.
59. Schoppet M, Shroff RC, Hofbauer LC, Shanahan CM. Exploring the biology of vascular calcification in chronic kidney disease: what's circulating? Kidney Int. 2008; 73(4):384–390. [PubMed: 18046319]
60. Gutierrez OM. Fibroblast growth factor 23 and disordered vitamin D metabolism in chronic kidney disease: updating the "trade-off" hypothesis. Clin J Am Soc Nephrol. 2010; 5(9):1710–1716. [PubMed: 20507957]

61. El-Abbadi MM, Pai AS, Leaf EM, et al. Phosphate feeding induces arterial medial calcification in uremic mice: role of serum phosphorus, fibroblast growth factor-23, and osteopontin. Kidney Int. 2009; 75(12):1297–1307. [PubMed: 19322138]

62. Faul C, Amaral AP, Oskouei B, et al. FGF23 induces left ventricular hypertrophy. J Clin Invest. 2011; 121(11):4393–4408. [PubMed: 21985788]

63. Mirza MA, Larsson A, Lind L, Larsson TE. Circulating fibroblast growth factor-23 is associated with vascular dysfunction in the community. Atherosclerosis. 2009; 205(2):385–390. [PubMed: 19181315]

64. Yilmaz MI, Sonmez A, Saglam M, et al. Comparison of Calcium Acetate and Sevelamer on Vascular Function and Fibroblast Growth Factor 23 in CKD Patients: A Randomized Clinical Trial. Am J Kidney Dis. 2012; 59(2):177–185. [PubMed: 22137672]

65. Autosomal dominant hypophosphataemic rickets is associated with mutations in FGF23. Nat Genet. 2000; 26(3):345–348. [PubMed: 11062477]

66. Dietary Reference Intakes for Water. Potassium, Sodium, Chloride, and Sulfate. The National Academies Press; 2005.

CLINICAL SUMMARY

- Sodium and phosphorus-based food additives have a wide diversity of applications in processed food, making them heavily utilized in the food manufacturing industry.
- The proportion of daily sodium and phosphorus intake that comes from food additives alone is substantial, and in the case of sodium, accounts for nearly 75% of total sodium intake per day in Westernized diets.
- Excess sodium and phosphorus intake have important links to cardiovascular and bone disease in chronic kidney disease, making food additives a major nutritional risk factor for adverse clinical outcomes in individuals with chronic kidney disease.
- Since current laws classify sodium and phosphorus-based food additives as generally safe for public consumption—essentially allowing them to be used with little to no restrictions by the food industry—this represents a major barrier to reductions in intake of excess sodium and phosphorus in individuals with chronic kidney disease.

Table 1

United States Department of Agriculture Dietary Reference Intakes for sodium and phosphorus intake by age group

Nutrient	Age	RDA/AI (grams/day)	TUL (grams/day)
Sodium[66]	0-6 months	0.12*	ND
	7-12 months	0.37*	ND
	1-3 years	1.0*	1.5
	4-8 years	1.2*	1.9
	9-50 years	1.5*	2.3
	50-70 years	1.3*	2.3
	> 70 years	1.2*	2.3
Phosphorus[37]	0-6 months	0.1*	ND
	7-12 months	0.28*	ND
	1-3 years	0.46	3.0
	4-8 years	0.5	3.0
	9-13 years	1.25	4.0
	14-18 years	1.25	4.0
	> 18 years	0.7	3.0

RDA, recommended daily allowance: defined as the average daily intake level sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in a group, calculated from the estimated average requirement (EAR) per day—if an EAR is not available because of lack of sufficient scientific evidence, an adequate intake level is developed instead; AI, adequate intake: defined as the recommended daily intake level based on observed or experimentally determined approximations of estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate; TUL, tolerable upper limit: defined as the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population.[37]

*Represents AI (RDA unable to be determined)