Scientific review article

Neglected importance of cumulative exposure to phosphorus in drinking water and food products

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ABSTRACT

Using a risk assessment approach possible health risks from different chemicals or other environmental stressors could be assessed. The method is widely used for regulatory risk assessment of chemicals. Although the method gives good results in the field of public and environmental health risk assessment, the approach has several flaws and unknowns, since disregarded real exposure scenarios could sometimes also lead to wrong assumptions. Using the risk assessment approach in the case of phosphate additives we will present weather added phosphorus in food and drinking water, presenting some concerns for human health. In recent years in developed countries, according to recent studies, intake of phosphorus and consequently phosphorus serum levels are increasing. Besides naturally present phosphates in food, predominantly pre-processed food and also processed (chemically softened) drinking water is a source of additional phosphate intake. The main reason for drinking water chemical softening is primarily prevention of the equipment; the health effect of such treatment is underestimated and neglected.

Although phosphorus is an essential element, according to latest researches blood vessel calcification and hormonal de-regulation as health effect of high phosphorus concentration are reported. Any kind of increased intake of phosphorus is therefore not needed and in fact it could actually present an additional health threat. Therefore it is necessary that a holistic approach of risk assessment is used in the context of realistic exposure scenarios of simultaneous exposure to cocktail of various pollutants, their degradation products, and inclusion of potential causal links and indirect impacts of evaluated chemicals on health.

According to the presented facts health risk in the case of sodium polyphosphate as drinking water softeners is insufficiently investigated and consequently, the risk might be underestimated.

Key words: risk assessment, polyphosphates, water softening

Received: 7.8.2014
Accepted: 30.9.2014

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INTRODUCTION

Understanding the risk for human health on the field of environmental and public health, mainly due to increasing environmental pollution with different chemicals, is essential to implement appropriate steps to ensure the health of the general population. Often there is not just one "answer" or one "approach" to the question of the risk assessment of substances in the environment [1]. Individuals (and the population) are exposed to various harmful factors in the environment, from which each of them could affect their health differently.

Most of the available information and data on the toxicological endpoints are, unfortunately, available only for one selected chemicals. This lack of information is followed by the traditional approach in risk assessment, which consequently focuses on the assessment of a single chemical, while ignoring the real exposure conditions (co-exposure to a cocktail of different compounds, their interaction and possible synergism or multiplicative effects, the effect of degradation by-products, side effects, and other). This is especially the case in the term of regulatory toxicology and registration of chemicals. Therefore need for a more holistic approach in human health risk assessment of chemicals is needed. Cumulative risk assessment as a tool for analyzing information to examine, characterize and possibly quantify combined threats from multiple environmental stressors [2-4] is one of the answers to these needs. Several studies confirm that exposure to multi-component chemical mixtures pose one common pattern, regardless of the specific chemicals, exposed organism or biological endpoint is observed: toxicity of a chemical "cocktail" is higher than the individual toxic effect of individual observed chemical compound. Same effect can be observed when low, individually non-toxic concentrations of chemicals can result in a sever toxicity, if they co-occur in a mixture. Unfortunately, there are rare studies [5] that take into account the real scenarios and environmentally relevant conditions (low concentrations, lifetime exposure, inclusion of chemical by-products and mixtures). The exposure scenario for intake into the body therefore should consider cumulative exposure from different products and/or media and/or pathways.

According to recent published studies [6-11] phosphorus intake, especially in developed countries, pose a health threat due to high consumption and consequently high serum concentration. High phosphorus serum concentration is related with health threats not only for specific endangers groups like CKD patients [12-14] but also for general population [6-8]. Additionally, the trend of phosphorus intake via everyday diet in developed countries is increasing [8, 15-16], especially due to the high amount of phosphorus additives in pre-processed food.

RISK ASSESSMENT APPROACH

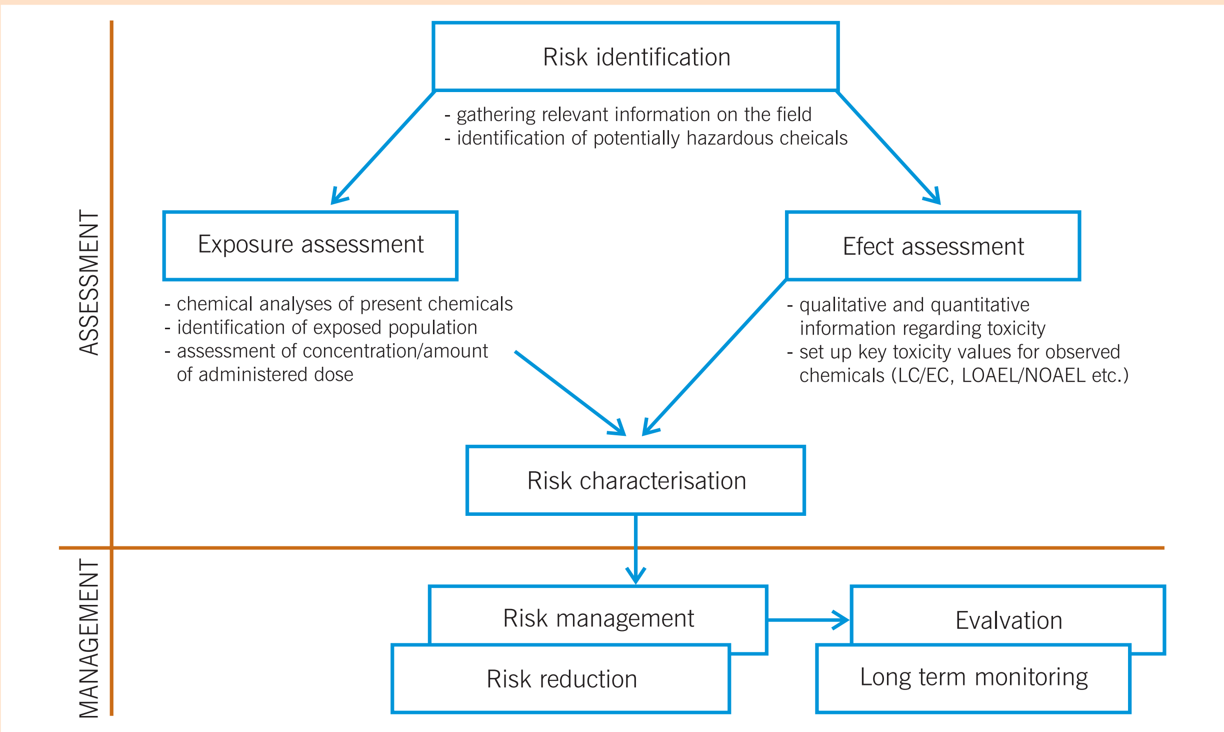
Risk assessment in the content of public health is, to the highest extent possible, a scientific process and represents the method for evaluation and quantification of the probability that harmful effect to individuals or populations from certain chemical or other stressor could occur. The classic approach to risk assessment is based on 4 steps:

1. Risk identification – risk has to be recognized and identified.
2. Hazard assessment and determination of the toxicity (determination of the concentration at which effects are not expected – NOAEL) for a selected chemical.
3. Exposure assessment. Hazard (toxicity) of chemicals does not mean that the deleterious effect on the organism occurred; crucial is contact/absorption in the organism. For exposure assessment data of concentration, route of administration, metabolism, bioavailability and concentration in the target organ is needed.
4. Risk characterization as the final step is done on the basis of the above mentioned steps taking into consideration appropriate safety factors. With such approach the limited values below which no harmful impacts are expected as well as threshold values and acceptable daily intake (ADI) values can be established.

The risk assessment approach should be followed by the risk management, with which we can manage, reduce, reuse, and take other safety measurement, continuous evaluation and correction of risk assessment.

Despite the positive intentions of the classical risk assessment method [1, 17-21] risk assessment approach has several flaws, confronts many unknowns and could sometimes also be based on wrong assumptions.

Figure 1:
Risk assessment approach



Besides neglecting already mentioned real exposure scenarios (especially long-term exposure to low concentration of mixtures) main flaw are related to the uncertainty of the results of toxicological and risk assessment studies (sampling errors, analytic errors, systematic errors, errors due to intra and inter-species extrapolation), influence of different root of exposure on toxic effect, (un)reliability of QSAR (Quantitative Structure Activity Relationship) and SAR (Structure Activity Relationship) models, unreliability of computer models (simplification of complex phenomena in the environment and in the body to linear mathematical models), disregard the impact of hormesis [22-24], multiplicative effects of different chemicals [25], the effects of synergism [26], and antagonism [26], disregarding the impact of degradation by-products, bioaccumulation and bioconcentration by the food chain [27-29], side effects from real case exposure scenarios (by-effects, collateral effects, indirect effect), cumulative effect of daily intake through different sources, and other less significant issues.

In order to show complexity and possible human health threats the case study of added phosphorus in food and drinking water is presented.

CASE STUDY: PHOSPHORUS IN DRINKING WATER

The main reason for drinking water softening is primarily prevention of the equipment such as hot-water boilers, kettles and pipes from limestone formation, especially in case when the source of drinking water is rather hard (carbonate hardness). The main reason for water softening is therefore economical; the health effect of such treatment might be underestimated and neglected. For softening there are several different approaches possible.

Figure 2:
Limestone formation in drinking water pipelines and hot water boilers

Figure 3:
Sodium polyphosphates dosage into the drinking water system

Usually in the domestic distribution network sodium and potassium salts are used, however also softening using sodium polyphosphates is rather common. According to Slovenian legislation [30] adding phosphates in drinking water is not allowed, however it is also not controlled.

Softening is mainly performed on warm, sometimes also in cold drinking water. It is performed on domestic water installation, usually before drinking water enters the boiler for heating.

PHOSPHORUS IN FOOD

Beside intake via drinking water majority of phosphates are ingested via different foods. Phosphorus as food additives is used in several formulations (phosphoric acid (E 338–341; E 343) and polyphosphates (E 450–452)) and is authorized in a large number of food products for several technological purposes. A maximum tolerable daily intake (MTDI) of 70 mg/kg of body weight (bw) of phosphorus was established by several authorities [31-33], however acceptable daily intake (ADI) was not able to be determined because phosphorus (primarily as phosphate) is an essential nutrient and an unavoidable constituent of food. Based on mentioned expertise limited values of phosphorus additives in different food products are determined [32, 34-35]. However for individual food product these levels are set rather high not including cumulative effect of the daily intake through different products.

In the last few decades therefore phosphorus intakes have risen significantly due to the greater use of phosphates as food additives in different food products [15]. The mean daily phosphorus intake of adults in European countries ranges between 1017 and 1422 mg [16] and between 1030 and 1727 mg for USA population [8], a level well above the current recommendations [8, 36]. Several scientific studies claims increased Phosphorus intake could be linked to several health problems [7, 37]; therefore EU food authorities (EFSA) will re-evaluate phosphates for use as food additives with high priority by the end of the year 2018 [11]. In the context of this re-evaluation all relevant toxicological information will be collected and re-evaluated.

Since phosphorus is an essential microelement and can be found in any cell, it is therefore also “naturally” present in all kinds of food products. However, in animal protein rich food phosphates are present mainly in the form of organic phosphate esters [6] which are slowly hydrolyzed and therefore relatively low absorption (40 – 60 %) is present [38-40]. Plants phytate are less bioavailable and therefore less than 50 % is absorbed [39-41]. On the other hand, for industrial processed food different additives are used, among many of them as polyphosphates or in the form of other inorganic phosphate salts which are almost entirely absorbed in gastrointestinal tract [40]. The same polyphosphate salts are used also in the process of water softening, where again phosphate “additives” are added in to the food (drinking water).

PHOSPHORUS IN EVERY DAY DIET AND HEALTH EFFECT

Phosphorus is an essential element and crucial for cells (and organisms) vital functions. It is widely present in all kinds of food, however according to latest research [6, 8] the amount of phosphorus intake has increased significantly in the last years which lead to unbalance phosphorus homeostasis in the organism. Several researchers [40, 42-46] reported the health effect of high phosphorus concentration among patients with chronic kidney disease, especially higher mortality [43, 45-46]. Recently researchers have stressed the correlation between cardiovascular diseases and high serum phosphorus concentration in the general population [6, 39, 44, 47]. High phosphate serum concentration caused vascular calcification in vitro and in vivo [44, 48].

More and more authors point out that it is necessary that the holistic approach of risk assessment is used in the context of realistic scenarios of simultaneous exposure to whole cocktail of various pollutants, their degradation products, a variety of comprehension and sensitivity of the individual exposed person, especially in the case of specific vulnerable groups and the inclusion of potential causal links and indirect impacts of evaluated chemicals on health. Therefore some additional approaches should be included in health risk assessment for phosphorus additives, especially holistic view on health effect, such as use of epidemiological data and collateral side effects which phosphorus might have (role of increased phosphorus concentration on hormonal regulation and vascular cell re-programination to osteoblast like cells) instead of assessment only narrow (especially acute) toxicity data.

CONCLUSION

Based on the arguments presented, human health risk assessment for exposure to water softeners (potassium polyphosphates) should be revised; possible interaction between different chemicals (synergism, antagonism, multiplicism) should be included as well as other indirect effects, as well as the effect of cumulative (daily) intake through different sources. Traditionally risk assessments (and also toxicological tests, based on which such risk assessment is made) are made for pure chemicals and ignore all of the above mentioned factors. It is urgent to review such approach in order to determine the interaction between different substances in water and water softeners and, consequently, the phenomenon of multiplication, synergism or antagonism.

As mentioned in the article several authors [8, 15-16] report about the correlation between high phosphorus intake, high serum concentration and health effects, not only among vulnerable groups but also among the general population. Any kind of additional intake of phosphorus is therefore not needed, in fact it could actually present an additional (phosphorus) burden and therefore additional health threat, which is also true in the case of using phosphates as drinking water softeners.

In case of intake of phosphorus the lack of information is crucial. The general public have not adequate knowledge about the potential risk to the cardiovascular system and renal function caused by high phosphorus consumption. Consumers usually also cannot decide for a product with lower phosphorus content due to poor food labelling. The same problems occur in case of drinking water softening, since consumers usually have no idea, that caretaker in their building use such chemical treatment of their drinking water. Usually intake of phosphorus via individual food products is not extremely high and could be negligible compared to the RDA (Recommended Dietary Allowance). In case of drinking water softening recommended values of polyphosphates are rather low compared to RDA for phosphorus daily intake, however it also contributes to the total sum of daily phosphorus consumption, therefore total daily intake of phosphorus could be (and in most cases is) extremely high and above the recommended values.

Based on the mentioned facts we estimate that the health risk in the case of sodium polyphosphate as a drinking water softener is insufficiently investigated and consequently, the risk is probably underestimated.

ACKNOWLEDGEMENTS

Financial support from the European Social Fund (ESF) and the Ministry of Education, Science and Sport of RS is gratefully acknowledged.

REFERENCES

[1] Patton D.E. 1993. The ABCs of risk assessment. EPA Journal 19, pp. 10–15.

[2] EPA (Environmental Protection Agency). 2003. Framework for Cumulative Risk Assessment. Washington, DC: EPA Risk Assessment Forum.

[3] Callahan M.A., Sexton K. 2007. If cumulative risk assessment is the answer, what is the question? Environ Health Perspect, 115(5), pp. 799–806.

[4] Sexton K. and Linder S.H. 2011. Cumulative Risk Assessment for Combined Health Effects from Chemical and Nonchemical Stressors. American Journal of Public Health, 101(S1), pp. S81-S88.

[5] Magnusson M., Heimann K., Quayle P., Negri A.P. 2010. Additive toxicity of herbicide mixtures and comparative sensitivity of tropical benthic microalgae. Marine Pollution Bulletin, 60 (11), pp. 1978–87.

[6] Ritz E., Hahn K., Ketteler M., Kuhlmann M.K., Mann J. 2012. Phosphate additives in food – a health risk. Dtsch Arztebl Int, 109(4): 49–55.

[7] Ellam T.J., Chico T.J. 2012. Phosphate: The new cholesterol? The role of the phosphate axis in non-uremic vascular disease. Atherosclerosis, 220(2), 310–8.

[8] Calvo M.S., Uribarri J. 2013. Public health impact of dietary phosphorus excess on bone and cardiovascular health in the general population. Am J Clin Nutr.

[9] Pravst I. 2011. Risking public health by approving some health claims? – the case of phosphorus. Food policy, 36: 726–8.

[10] Uribarri J., Calvo M.S. 2003. Hidden sources of phosphorus in the typical American diet: does it matter in nephrology?. Seminars in Dialysis, 16(3): 186–8.

[11] EFSA. 2013. Assessment of one published review on health risks associated with phosphate additives in food. EFSA Journal, 11(11), p. 3444.

[12] Winger R.J., Uribarri J., Lloyd Lyn. 2012. Phosphorus – containing food additives: an insidious danger for people with chronic kidney disease. Trends in Food Science and Technology, 24: 92–102.

[13] Sherman R.A., Mehta O. 2009b. Phosphorus and potassium content of enhanced meat and poultry products: implications for patients who receive dialysis. CJASN, 4: 1370–3.

[14] Sherman R.A., Mehta O. 2009a. Dietary phosphorus restriction in dialysis patients: potential impact of processed meat, poultry and fish products as protein sources. American Journal of Kidney Diseases, 54(1): 18–23.

[15] Calvo M.S., Park, Y.K. 1996. Changing phosphorus content of the US diet: potential for adverse effects on bone. Journal of Nutrition.

[16] Elmadfa I. 2009. European Nutrition and Health Report.

[17] EPA. 1989. Risk Assessment Guidance for Superfund - Volume I. Human Health Evaluation Manual (Part A) – Interim Final. Office of Emergency and Remedial Response, U.S. Environmental Protection Agency, Washington, ZDA.

[18] EPA. 2011. EPA Risk Assessment: Basic Information. Dostopno na: http://epa.gov/riskassessment/basicinformation.htm#risk [dostopno 12.01.2012]

[19] Asante-Duah K. 2002. Public health risk assessment for human exposure to chemicals. Kluwer Academic Publisher, Dordrecht, Boston, London.

[20] Leeuwen C. J., van Vermeire T. 2007. Risk assessment of chemicals: an introduction, 2nd ed.

[21] Robson M. G. and Toscano W. A. 2007. Risk assessment for environmental health. John Wiley & Sons, Inc, ZDA.

[22] Fukushima S., Kinoshita A., Puatanachokchai R., Kushida M., Wanibuchi H. and Morimura K. 2005. Hormesis and dose-response-mediated mechanisms in carcinogenesis: evidence for a threshold. Carcinogenesis, 26, pp. 1835–45.

[23] van Wyngaarden K.E. and Pauwels E.K. 1995. Hormesis: are low doses of ionizing radiation harmful or beneficial? Eur J Nucl Med, 22, pp. 481–6.

[24] Calabrese V., Cornelius C., Dinkova-Kostova A.T., Calabrese E.J., and Mattson M.P. 2010. Cellular Stress Responses, The Hormesis Paradigm, and Vitagenes: Novel Targets for Therapeutic Intervention in Neurodegenerative Disorders. Antioxidants & Redox Signaling, 13 (11), p: 1763-1811. doi:10.1089/ars.2009.3074.

[25] Yang J., Cao J., Sun X., Feng Z., Hao D., Zhao X., Sun C. 2011. Effects of long-term exposure to low levels of organophosphorous pesticides and their mixture on altered antioxidative defense mechanisms and lipid peroxidation in rat liver. Cell Biochem Funct. doi: 10.1002/cbf.182526.

[26] Berry W.L. and Wallace A. 1981. Toxicity: The concept and relationship to the dose response curve. Journal of Plant Nutrition, 3(1-4), p: 13-19; Special Issue: Trace Element Stress in Plants: Effects and Methodology

[27] Franke C., Studinger G., Berger G., Böhling S., Bruckmann U., Cohors-Fresenborg D. and Jöhncke U. 1994. The assessment of bioaccumulation. Chemosphere, 29 (7), pp. 1501–1514.

[28] LeBlanc G.A. 1995. Trophic-Level Differences in the Bioconcentration of Chemicals: Implications in Assessing Environmental Biomagnification. Environ. Sci. Technol., 29 (1), pp. 154–160.

[29] Hu G., Dai J., Xu Z., Luo X., Cao H., Wang J., Mai B., Xu M. 2010. Bioaccumulation behavior of polybrominated diphenyl ethers (PBDEs) in the freshwater food chain of Baiyangdian Lake, North China. Environment International, 36 (4), pp. 309–315.

[30] Rules on drinking water (Pravilnik o pitni vodi), Uradni list RS, št. 19/04, 35/04, 26/06, 92/06 in 25/09.

[31] JECFA (Joint FAO/WHO Expert Committee on Food Additives). 1982. Evaluation of certain food additives and contaminants (Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 683.

[32] JECFA (Joint FAO/WHO Expert Committee on Food Additives). 2012. Safety evaluation of certain food additives / prepared by the Seventy-sixth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series.

[33] SCF (Scientific Committee for Food). 1991. First series of food additives of various technological functions. Available online: http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_25.pdf

[34] Union list of food additives in Annex II of Regulation (EC) No 1333/2008.

[35] Regulation (EC) No. 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives

[36] IVZ, 2013. Referenčne vrednosti za vnos vitaminov in mineralov – tabelarična priporočila za otroke, mladostnike, odrasle in starejše. Ljubljana, p. 7.

[37] McCarty M.F., DiNicolantonio J.J. 2014. Bioavailable dietary phosphate, a mediator of cardiovascular disease, may be decreased with plant-based diets, phosphate binders, niacin, and avoidance of phosphate additives. Nutrition, 30(7–8), pp. 739–747.

[38] Sullivan C., Sayre S.S., Leon J.B., Machekano R., Love T.E., Porter D., Marbury M., Sehgal A.R. 2009. Effect of food additives on hyperphosphatemia among patients with end stage renal disease: a randomized controlled trial. JAMA, 301(6): 629–35.

[39] Tonelli M., et al. 2005. Relation between serum phosphate level and cardiovascular event rate in people with coronary disease. Circulation, 112: 2627–33.

[40] Noori N, Kalantar-Zadeh K., Kovesdy C.P., Bross R., Benner D., Kopple J.D. 2010. Association of dietary phosphorus intake and phosphorus to protein ratio with mortality in hemodialysis patients. CJASN, 5(4): 683–92.

[41] Lei X.G., Porres J.M. 2003. Phytase enzymology, applications, and biotechnology. Biotechnol Lett, 25: 1787–94.

[42] Block G.A., Hulbert Shearon T.E., Levin N.W., Port F.K. 1998. Association of serum phosphorus and calcium x phosphate product with mortality risk in chronical hemodialysis patients: a national study. Am J Kidney Dis, 31: 607–17.

[43] Block G.A., et al. 2004. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. JASN, 15: 2208–18.

[44] Foley R.N., Collins A.J., Herzog C.A., IShani A., Kaira P.A. 2009. Serum phosphorus levels associate with coronary atherosclerosis in young adults. JASN, 20: 397–404.

[45] Kestenbaum B., Sampson J.N., Rudser K.D., Patterson D.J., Seliger S., Young B., Sherrard D.J., Andress D. 2005. Serum phosphate levels and mortality risk among people with chronic kidney disease. JASN, 16: 520–8.

[46] KDIGO. 2009. Clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl, S1 – 130.

[47] Dhingra R., et al. 2007. Relations of serum phosphorus and calcium levels to the incidence of cardiovascular disease in the community. Arch Intern Med, 167: 879–85.

[48] Giachelli C.M. 2009. The emerging role of phosphate in vascular calcification. Kidney Int, 75: 890–7.