BDA The Association of UK Dietitians

Renal Nutrition Specialist Group

Phosphorus in Foods: Considerations in Chronic Kidney Disease

An evidence-based summary

Contents

1. Summary

Dietary intervention is a key factor in the management of hyperphosphataemia in Chronic Kidney Disease (CKD) and the specialist renal dietitian has a fundamental role to play in the provision of consistent and relevant dietary information.

To support this, a working group of the British Dietetic Association - Renal Nutrition Group (BDA-RNG) have conducted a review of the current available evidence base and have formulated recommendations for dietary phosphate management in CKD (Hannah et al, 2017). In view of the lack of systematic reviews and high-quality studies in the current literature, the recommendations provided are limited to current international guidelines, available data and the expert opinions of the authors of this document.

In order to provide informed and appropriate dietary modifications, it is important that dietitians and patients have knowledge and awareness of dietary sources of phosphate. This paper outlines the known dietary sources of phosphorus, the contribution from phosphorus containing food additives and the varying bioavailability of phosphates. It describes the challenges faced by renal dietitians and renal patients in controlling serum phosphate levels and the potential for improvements to the provision of dietary information in this important area.

2. Background

The terms phosphate and phosphorus are often used interchangeably and this can lead to confusion. Phosphorus is a highly reactive element, so it is usually found in combination with other elements or molecules. Phosphate is produced when phosphorus and oxygen combine. The majority of the phosphorus in the human body (70-85%) combines with calcium to form hydroxyapatite in bones and teeth. The remainder is stored in soft tissues in various forms e.g. within the nucleic acids DNA and RNA, phospholipids, adenosine triphosphate (ATP), creatine phosphate, phosphorylated sugars and proteins, and a small amount is complexed with sodium, calcium and magnesium as salts in the blood. Only 1% of total body phosphorus circulates in the blood as both organic and inorganic phosphates, therefore serum phosphate measurements do not reflect total body stores of phosphorus.

The balance of phosphorus in the body is controlled by complex interactions involving phosphorus absorption, bone turnover, renal excretion and intestinal secretion and is regulated by calcium, active vitamin D (1,25 (OH)2D), fibroblast growth factor 23 (FGF23) and parathyroid hormone (PTH). Serum phosphate levels are influenced by a circadian rhythm, as well as diet, with lowest levels found in the morning, a small rise in the afternoon, followed by a nocturnal peak (Vervloet et al, 2017). It is thought that the morning low is due to movement of phosphate into the intracellular space (Vervloet et al, 2017).

In the latter stages of CKD phosphate retention and disturbances in calcium and phosphorus homeostasis are common. This can lead to the development of CKD mineral and bone disorder (CKD–MBD), a syndrome that includes secondary hyperparathyroidism, renal bone disease (renal osteodystrophy), vascular and soft tissue calcification, arterial stiffness and atherosclerosis. As a result, hyperphosphataemia is associated with an increased prevalence of cardiovascular disease and increases the risk of all-cause mortality in this population (KDIGO, 2017). The first line management of hyperphosphataemia is dietary; the National Institute for Health and Care Excellence (NICE, 2013) recommend that all patients with hyperphosphataemia should receive individualised information and advice on phosphate management from a specialist renal dietitian.

3. Introduction

An Adequate Intake (AI) of phosphorus, for adults in the general population, is considered to be 550 mg/day (EFSA, 2015). The European Food Safety Authority (EFSA, 2015) have estimated that phosphorus intake in the European countries is 1000-1767 mg/day. It has been suggested that dialysis patients in the USA consume between 1000-2000 mg/day (Noori et al, 2010). Historically it was suggested that the upper limit of a phosphorus restricted diet, for those on haemodialysis, should be 800-1000 mg/day (Fouque et al, 2007); this was based on expert opinion, and is difficult to both assess and achieve. This figure was revised to 1000-1400 mg/day for those on haemodialysis or peritoneal dialysis (EDTNA/ERCA, 2012). Kidney Disease: Improving Global Outcomes (KDIGO, 2017) did not state a specific limit and states that "aggressive dietary phosphorus restriction is difficult because it has the potential to compromise an adequate intake of other nutrients, especially protein".

It is important to consider the source of phosphorus when making dietary recommendations in the management of hyperphosphataemia (KDIGO, 2017). Phosphorus is found in nearly every food and is derived from three main groups:

- Animal foods (mainly organic phosphorus, found in proteins and deoxyribonucleic acid (DNA))
- Plant foods (mainly organic phosphorus as phytates and proteins)
- Foods and drinks containing food additives (mainly inorganic phosphorus)

Dietary intervention has previously focused on limiting organic phosphorus from protein-based foods (Kalantar-Zadeh, 2013; St-Jules et al, 2016). Recently, there has been a shift in this focus, based on increased knowledge of the differing bioavailability across the three main groups of phosphorus sources, an increase in the use and consumption of phosphorus containing food additives, as well as evidence regarding the increased mortality risks from an insufficient dietary protein intake in this patient group (Naylor et al, 2013). Therefore, dietary intervention should emphasise the importance of ensuring an adequate protein intake when limiting dietary phosphorus. NICE states that specialist renal dietitians should "give information about controlling intake of phosphate-rich foods (in particular, foods with a high phosphate content per gram of protein, as well as food and drinks with high levels of phosphate additives) to control serum phosphate, while avoiding malnutrition by maintaining a protein intake at or above the minimum recommended level" (NICE, 2013).

4. Sources of dietary phosphorus

Phosphorus is found in nearly every food and is derived mainly from proteins, phytates and food additives. It is found in both organic and inorganic forms.

4.1. Organic phosphorus

Organic phosphorus is found in animal proteins such as casein and also in plant foods such as phytate. In protein foods, phosphorus is found as a constituent of phosphoproteins, phospholipids, adenosine diphosphate (ADP) and adenosine triphosphate (ATP), deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Organic phosphorus is also present in plant foods; however, most of the phosphorus is bound to phytates and requires phytase to break this bond in order to release the phosphorus.

4.1.1. Animal foods

Animal-based foods are rich in organic phosphorus as it is an abundant component in animal tissues and proteins, e.g. casein. In a non-vegetarian western diet, over one-half of dietary phosphorus originates from animal proteins (Noori et al, 2010).

4.1.2. Plant foods

Phosphorus is present as phytate in the outer coating of cereal grains, seeds, nuts and pulses (Calvo et al, 2012). Phytate (Myo-inositol-1,2,3,4,5,6-hexakisphosphate) is the major storage form of phosphorus, energy and minerals in seeds and other plant tissues.

Phytases are phosphorolytic enzymes which catalyse the release of phosphorus from phytate. They are present in plants, micro-organisms and some animal tissue but are not present in the human gastrointestinal (GI) tract. During the germination of seeds, phytases catalyse the release of phosphorus and other minerals so that they become available for the development of seedlings. However, in food processing and heat treatment, phytases are most likely to be inactivated (Williams et al, 2013).

4.1.3 Alcoholic drinks

There is a significant amount of phosphorus bound to phytic acid in grape seeds. During the production of wine phosphorus is released into the wine by maceration of the skins and seeds followed by fermentation.

In the brewing of beers, the fermentation process releases phosphorus from the grains, but the final phosphorus content varies due to differences in the malting and mashing processes. For example, lagers usually contain more phosphorus than beers, due to the differences in these processes. There is no difference in the phosphorus content of low alcohol beers and lagers.

The phosphorus present in beer and wine can come from these natural ingredients. Red wine and Pilsner beers usually have more phosphorus than other alcoholic drinks. (Lindley et al, 2014). Red wines generally have a higher phosphorus content than white wines. Some white wines have been found to have a higher phosphorus content. This is thought to be due to the addition of di-ammonium phosphate if there is insufficient nitrogen in the crushed grape juice, increasing the phosphorus content of these drinks (Lindley et al, 2014). Alcoholic beverages containing more than 1.2 % by volume of alcohol are exempted from the mandatory listing of ingredients and therefore any additives used are not declared.

4.2. Inorganic phosphorus

Inorganic phosphorus is present in many food additives (Kalantar-Zadeh, 2013). The amount of phosphorus contributed by food is rising due to the increasing use of phosphorus-containing ingredients in manufacturing and food processing (KDIGO, 2017). It is thought that the amount of phosphorus added to food has doubled since the 1990’s (Ritz et al, 2012). In total, it is estimated that a diet including phosphorus containing additives can increase intake by 600-800mg (Carrigan et al, 2014; León et al, 2013).

4.2.1. Phosphorus containing food additives

The use of food additives in the UK and the European Union (EU) is strictly regulated under European law. Additives must be approved as safe by the European Food Safety Authority (EFSA) before they can be used and maximum amounts are decided on the basis of a safety evaluation. Phosphorus containing additives, like other additives, are used in small quantities in a range of food and drink products to help maintain the quality and safety of food.

In addition to the rigorous safety assessment and maximum usage limits on specific additives in defined food categories, an additive may only be used if a manufacturer can demonstrate the following requirements:

I. there is reasonable technological need and the purpose cannot be achieved by other means which are economically and technologically practical
II. they present no hazard to the health of the consumer at the level of use proposed, so far as can be judged on the scientific evidence available
III. they do not mislead the consumer.

The current maximum levels of additive use are based on the former EU Scientific Committee for Food (SCF) recommendations.

The current authorisation for phosphates in the EU requires them to be labelled where they are used. A food additive that is authorised and included in the Annex II of the Regulation 1333/2008 is required to be identified on the food label by name and E number e.g. Phosphoric Acid, E338 or by their category and name or E number e.g. Acidity Regulator, E338 or Acidity Regulator, Phosphoric Acid (European Commission, 2008). Additives identified by their category and E number alone are difficult to identify as phosphorus containing.

Table 1. This table outlines the main phosphorus containing food additives permitted in the EU. These additives may contribute significantly to the phosphorus content of foods (European Commission, 2008). The RNG recommends that renal dietitians encourage patients, where possible, to limit foods containing these additives (Hannah et al, 2017)

E- number	Name of additives	Products	Technical functions
E338	Phosphoric acid	Non-alcoholic flavoured drinks Sterilised and UHT milk Candied fruits Fruit preparations Beer Processed meats Sweets, cakes and chocolate	Acidity regulator Antioxidant synergist
E339	Sodium phosphates E339 (i) Monosodium phosphate E339 (ii) Disodium phosphate E339 (iii) Trisodium phosphate	Partly dehydrated milk Dried milk powder pasteurised, sterilised and UHT cream Whipped cream and vegetable fat analogues Unripened cheeses Canned soup Breaded chicken and fish	Acidity regulator Sequestrant Emulsifier Texturiser Stabiliser Water retention agent
E340	Potassium phosphates E340 (i) Monopotassium phosphate E340 (ii) Dipotassium phosphate E340 (iii) Tripotassium phosphate	Processed cheese Meat products Sports drinks and prepared Table waters Vegetable protein drinks Powdered milk Desiccated coconut	Acidity regulator Sequestrant Emulsifier Texturiser Stabiliser Water retention agent
E341	Calcium phosphate E341 (i) Monocalcium phosphate E341 (ii) Dicalcium phosphate E341 (iii) Tricalcium phosphate	Beverage whiteners Edible ices Desserts Milk desserts Powdered milk Dry powder for dessert mixes Self-raising flour Instant pasta Sauces	Acidity regulator Flour treatment agent Firming agent Texturiser Rising agent Anticaking agent Water retention agent Source of calcium
E343	Magnesium phosphate E343 (i) Monomagnesium phosphate E343 (ii) Dimagnesium phosphate	Bakery products Flour Liquid egg Salt substitutes Prepared mustard	Acidity regulator Anticaking agent
E450	Diphosphates E450 (i) Disodium diphosphate E450 (ii) Trisodium diphosphate E450 (iii) Tetrasodium diphosphate E450 (v) Tetrapotassium diphosphate E450 (vi) Dicalcium diphosphate E450 (vi) Calcium dihydrogen diphosphate	Bakery products Meat products Processed cheese Sauces Soups and broths Instant tea and instant herbal infusions Edible ices Dried powdered food Milk based drinks	Emulsifier Stabiliser Acidity regulator Rising agent Sequestrant Water retention agent

		Baking powders	
E451	Triphosphates E451 (i) Pentasodium triphospshate E451 (ii) Pentapotassium triphospshate	Meat products Fish and seafood Processed cheese Beverage whiteners Edible ices Icing sugar Flavoured syrups for ice creams or milkshakes	Sequestrant Acidity regulator Texturiser
E452	Polyphosphates E452 (i) Sodium polyphosphate E452 (ii) Potassium polyphosphate E452 (iii) Sodium calcium polyphosphate E452 (iv) Calcium polyphosphate	Meat products Frozen fish and seafood Processed cheese Sauces (especially cheese based) Beverage whiteners Edible ices Icing sugar Sugar confectionary Dried powdered foods Milk based drinks Noodles Batters Processed potato products	Emulsifier Stabiliser Acidity regulator Rising agent Sequestrant Water retention agent

Box 1 further details key foods where these phosphorus-containing additives may be found. It is important to note that the presence of these additives in foods is brand related. Signposting patients to check the ingredient lists for these foods and drinks may help to identify which brands and products contain phosphorus containing additives.

Box 1. Key foods and drinks where phosphorus containing food additives may be found:

- **Bakery products:** cakes, biscuits, pastries and flour tortillas
- **Meat and poultry products**: processed meats, processed poultry, burgers, sausages and meat paste
- **Seafood products:** frozen processed and unprocessed fish, frozen processed and unprocessed shellfish and fish paste
- **Dairy products:** evaporated milk, creams, sterilised and ultra-high temperature processing (UHT) milk, dried milk products, milk desserts and yoghurt
- **Processed cheese:** spreadable and sliced processed cheese
- **Potato products:** frozen, chilled and dried products (e.g. chips, waffles, roast potato and mashed potato)
- **Dried powdered food items:** sauces (especially cheese-based), dessert mixes, soups, instant pasta dishes, instant noodles and dried milk
- **Non-alcoholic drinks:** dark fizzy drinks, soft drinks, and chocolate and malt dairy-based drinks

Table 2. This table outlines other authorised food additives that contain phosphorus. We understand that the contribution of phosphorus from these additives is likely to be less significant (European Commission, 2008). The RNG recommends that there is no requirement to focus on these additives in the management of hyperphosphataemia.

E- number	Name of additives	Products	Technical functions
E 101 (ii)	Riboflavin-5′-phosphate	Jams Milk products Sweets	Colour
E 322	Lecithin	Chocolate Mayonnaise Ice cream Margarine Processed baked goods	Antioxidant Emulsifier
E 442	Ammonium phosphatides (Phosphorus content not more than 3.4%)	Baked goods Alcoholic beverages Condiments Desserts Baking powder Frozen desserts Margarine Whipping cream toppings Yeast foods	Emulsifier
E 541	Sodium aluminium phosphates E 451 (i) Sodium aluminium phosphate-Acidic E 451 (ii) Sodium aluminium phosphates-Basic	Bakery products Processed cheese	Acidity regulator Emulsifier
E 626-635	Ribonucleotides		Flavour enhancer
	E 626 Guanylic acid	Instant noodles Potato crisps Savoury rice Tinned vegetables Cured meats Packet soups	
	E 627 Disodium 5’-Guanylate	Instant noodles Potato crisps Savoury rice Tinned vegetables Cured meats Packet soups	
	E 628 Dipotassium 5’-Guanylate	Products marketed as low-salt	
	E 629 Calcium 5’-Guanylate	Instant noodles Potato crisps Savoury rice Tinned vegetables Cured meats Packet soups	
	E 630 Inosinic acid	Processed soups and sauces	

	E 631 Disodium 5'-Inosinate	Potato crisps, instant noodles	
	E 632 Potassium Inosinate	Yeast extract, sardines	
	E 633 Calcium 5'-Inosinate	Processed meats and fish	
	E 634 Calcium 5'-Ribonucleotides	Products marketed as low-salt	
	E 635 Disodium 5'-Ribonucleotides	Products marketed as low-salt	

4.2.2. Modified starches

The authorisation for phosphates in food products in the EU requires them to be labelled where they are used, except in the case of modified starches where food labelling law specifies that they may be declared under the generic title of 'modified starches' on the ingredient list. There are 18 permitted modified starches of which only 5 contain phosphate (See Table 3) meaning that these phosphorus-containing additives cannot be identified using the food label. However, the contribution of phosphorus from modified starches is thought to be very low as they only contain residual phosphates (European Commission, 2008). Due to the low phosphorus load and the inability to identify phosphorus containing modified starches the RNG recommends not focusing on modified starches in dietary phosphate management.

Table 3. This table outlines the modified starches that contain phosphorus

E- number	Name of additives	Products	Technical functions
E 1410	Monostarch phosphate	Ice cream Pizza Battered fish Salad dressings	Stabiliser Thickener Binder
E 1412	Distarch phosphate	Jelly sweets Ready-made batter mixes	Stabiliser Thickener Binder
E 1413	Phosphated distarch phosphate	Batters for frozen foods Custards Sauces, mayonnaise and salad dressing Pies and fillings Instant beverages Dried foods Drinking yoghurts Flavoured milk Whipped cream Coffee Precooked pasta and noodles Starch-based puddings	Stabiliser Thickener Binder
E 1414	Acetylated distarch phosphate		Emulsifier Thickener
E 1442	Hydroxypropyl distarch phosphate		Stabaliser Thickener

4.2.3. Processing aids

Processing aids, including filtration aids and release agents, defined in Article 3.2 (b), are excluded from the scope of Commission Regulation 1333/2008. In the UK, there is no national legislation on processing aids nor is there any legally defined list of approved processing aids either within the UK or within the EU.

"Processing aid" means any substance which:

I. is not consumed as a food by itself;
II. is intentionally used in the processing of raw materials, foods or their ingredients, to fulfil a certain technological purpose during treatment or processing; and
III. may result in the unintentional but technically unavoidable presence in the final product of residues of the substance or its derivatives provided they do not present any health risks and do not have any technological effect on the final product.[1]

Processing aids may perform a number of functions in the food production process. For example, some serve to enhance food safety by reducing potential contamination in food during processing (antimicrobials) or facilitating an easier removal of impurities (flocculants)[2].

Processing aids sometimes contain phosphorus that remains after processing and is therefore present in the finished food, but only at safe and insignificant levels. Processing aids are not considered food additives and are not declared on food labels.

4.2.4. Re-evaluation of phosphates authorised as food additives in the European Union

Phosphorus containing additives are scheduled to be re-evaluated by EFSA in 2018. In 2017 EFSA called for usage data from the food industry and all relevant up-to-date scientific evidence on their toxicity will be collated and evaluated. The BDA - RNG is registered as an interested party and is therefore involved in this review process. The RNG collaborated with the British Renal Society, the BDA Paediatric Renal Interest Group (PRING) and the Irish Nutrition and Dietetic Institute, Renal Interest Group (IRIG) to use this opportunity to add our insights and to submit recommendations for EFSA to consider as part of the re-evaluation (See appendix 1 for an outline of the recommendations made by the RNG) (BDA-RNG, 2017).

5. The impact of phosphorus containing additives on phosphorus intake

A number of studies have sought to demonstrate the impact of additive use on potential phosphorus intake. McCutcheon et al (2015) examined the nutrition labels of 3000 of the best-selling foods and beverages and identified phosphorus additives to be present in 44% of the products reviewed. Uncooked meats and poultry products have 60% higher phosphorus content if enhanced (Sherman et al, 2009) and additive-enriched cooked ham contains 66% more phosphorus (Cupisti et al, 2012). Another study analysed the amount of phosphorus in 56 pairs of similar food products (one with and one without phosphorus additives) and found that products containing phosphorus additives contained approximately 60% more phosphorus than those with no additives (178±202 mg/100g vs. 111±112 mg/100g). However, the absolute and relative differences in phosphorus content varied substantially both between and within food product categories. For example, the difference in phosphorus among cheese products (n = 4 pairs) was +347 mg/100 g (+85%) (Leon et al, 2013).

Additive-free foods have been reported as being more expensive than their phosphorus containing counterparts (León et al, 2013). Where patients with CKD purchase these low-cost popular grocery foods in preference to other foods, they may unknowingly increase their risk of hyperphosphataemia.

[1] http://www.food.gov.uk/sites/default/files/multimedia/pdfs/guidance/food-additives-legislation-guidance-to-compliance.pdf
[2] http://www.foodinsight.org/Questions_and_Anwers_about_Processing_Aids_Used_in_Modern_Food_Production

A review article of observational studies suggested that high intakes of phosphorus from food additives increased the risk of cardiovascular disease in the general population as well as those with CKD (Ritz, 2012). The authors called for the quantity of phosphorus added to foods and drinks to be stated on food labels, as these additives potentially cause harm. This prompted statements in response by the European Food Safety Authority (EFSA, 2013), the International Food Additive Council (IFAC) and Phosphoric Acid & Phosphates Producers Association (PAPA), who concluded that due to the limitations in the design of those studies reviewed, links between high serum phosphate levels and increased cardiovascular risk in the general population could not be made (EFSA, 2013; IFAC & PAPA, 2012). They commented that CKD affects only a small proportion of the population and, that if required, food labels can be used to determine if phosphates are added to foods and drinks using the ingredient list (IFCA & PAPA, 2012).

Although dietitians can support patient awareness and knowledge of phosphates in foods, for example by encouraging patients to check ingredients lists and by providing them with ‘shopping cards’ which identify those additives to look out for on food labels, this may be too onerous for many of our patients to manage.

See appendix 2 for an example shopping card which lists the main phosphorus containing food additives permitted in the EU, and which has a message for patients to “look out for PHOS”. The “look out for PHOS” message will cover all of the main additives and although it will also include some of those which contribute less phosphorus, it is the easiest method of helping patients identify these additives.
The RNG is currently campaigning to improve food labelling for foods with added phosphorus to allow easy identification and to give patients an opportunity to make informed choices.

6. Phosphorus containing medications and dietary supplements

Dietary supplements and over-the-counter or prescription medications, such as antacids and laxatives, as well as some commonly used medications such as anti-hypertensives, may contain phosphate salts within their inactive ingredients (Calvo et al, 2014; Sherman et al, 2015). The data on the amount of phosphorus in oral medications and vitamin/mineral supplements is limited, but they may contribute to the phosphorus load (KDIGO, 2017). For example, Amlodipine and Lisinopril may contain up to 40mg of phosphorus per tablet and a similar amount is in a vitamin tablet marketed specifically for dialysis patients (Sherman et al, 2015).

Considering that total phosphorus intake is likely to be greater than 1000mg/day, the impact of medications and dietary supplements on phosphorus intake is likely to be low; the greatest source of easily absorbed phosphorus is more likely to be phosphorus containing food additives.

7. Considerations in dietary phosphate management

7.1. Phosphorus-to-protein ratio

Protein rich foods were previously thought to be the main source of dietary phosphorus in a typical mixed diet. While it is important to minimise the dietary phosphorus burden, a high dietary protein intake should be maintained in dialysis patients to avoid protein wasting and improve survival. One proposed way of balancing dietary phosphorus and protein intake is by using the phosphorus-to-protein ratio, which informs the selection of those dietary protein sources with the least serum phosphorus “cost.” (Kalantar-Zadeh, 2013). For example, egg white has one of the lowest phosphorus (P)–to-protein ratios (1.42mg P/g protein).

The phosphorus-to-protein ratio differs markedly depending on the food source. A high phosphorus-to-protein ratio was found to be associated with an increased mortality risk in patients on HD; the risk being the greatest in those who maintain a total dietary phosphorus-to-protein ratio >16mg P/g protein (Noori et al, 2010).

7.2. Limitations of nutrient data tables

Studies examining dietary phosphorus-to-protein ratio base their outcomes on data from current nutrient tables, which have several significant limitations.

- Nutrient data tables are likely to underestimate the phosphorus content of some foods as they may mostly reflect the organic phosphate content of foods (KDIGO, 2017).
- Analysis of foods is usually from pooled samples; some of which may contain phosphorus containing food additives, whereas some may not. The variation between similar products makes it impossible for patients and dietitians to accurately estimate the phosphorus content (Sullivan et al, 2007).
- For example, the phosphorus content of processed meats may be underestimated as they frequently contain phosphate additives (Leon et al, 2013; Carrigan et al, 2014). The analysis may underestimate phosphate by as much as 70% (Benini et al, 2011).
- Nutrient data tables cannot distinguish between inorganic and organic phosphorus. Hence the tables are likely to over or under estimate the phosphorus bio-availability and load.
- There is likely to be an overestimate of the bio-available phosphorus in foods high in phytates, particularly those that are uncooked.

7.3. Digestion, absorption and bioavailability of phosphorus

The bioavailability of phosphorus depends on the degree of digestibility of the food, the presence of compounds that can bind to phosphorus inhibiting its absorption (e.g. calcium, magnesium, aluminium) and the degree of vitamin D receptor activation in the GI tract (Cupisti et al, 2013).

The rate of phytate degradation in the human GI tract is low as humans lack the phytase enzyme. It mainly takes place by intestinal flora or non-enzymatic hydrolysis reactions (Cupisti et al, 2013). As a result, wholegrain foods and nuts have low phosphorus bioavailability (between 20 and 50%) (Kalantar-Zadeh, 2013; Williams et al, 2013). The total phosphorus content and bioavailability of phosphorus from multigrain products and legumes are variable and highly dependent on the method of food preparation.

The rate of digestion of organic phosphorus from animal foods is higher than that from phytate containing foods as it is more easily broken down by hydrolases in the intestinal tract. About 40% to 60% of animal-based phosphate is absorbed, depending on the GI vitamin D receptor activations (KDIGO, 2017).

Inorganic phosphorus in the form of food additives is the most readily absorbed source of phosphorus, with a bioavailability of 90 - 100% (Williams et al, 2013; Kalantar-Zadeh, 2013).

7.4. Studies of phosphorus absorption

In vitro studies

Two studies measured both the total phosphorus and digestible phosphorus in selected foods. Samples of these foods were digested enzymatically, replicating digestion in the alimentary canal, before phosphorus analysis. Better phosphorus digestibility was found in meat and milk products than in legumes and the greatest digestibility was found in foods and drinks with phosphorus additives. For example, muffins (containing sodium phosphate as a leavening agent) produced 100% phosphorus digestibility; for cola drinks and beer this was between 87% and 100%; for legumes this was 38% and for sesame seeds (with hull intact) only 6% of the total phosphorus was digestible (Karp et al, 2012).

Animal studies

One study looked at differences in phosphorus absorption in 24 rats with early but established CKD, who were fed either a casein-based diet (n=15) or a grain-based protein diet (n=9) both of which had the same total phosphorus content. They found that those fed a casein-based diet showed elevated level of FGF23 and urinary phosphorus excretion compared with those fed a grain diet. 60% of the phosphorus in the grain diet was in the form of phytate, whereas the casein diet was devoid of phytate, so all the phosphorus was bioavailable (Moe et al, 2009).

Absorption of phosphorus appears to take place via both an active transport system (Pep T1) and from passive absorption. In studies using rat models with CKD, a high phosphate diet has been found to increase the expression of PepT1 and the conclusion was that the dietary phosphorus levels regulated the intestinal peptide transport activity through Pep T1 (Furutani et al, 2013).

Human studies
A small, short term randomised study looked at differences in phosphorus absorption in 16 young healthy women. The subjects were randomised to five controlled 24-hour study sessions, each subject serving as her own control. At the control session, calcium intake was about 250 mg and phosphorus intake about 500 mg. For each of the other four study sessions, 24-hour phosphorus intake was about 1500 mg, 1000 mg of which was obtained from either meat, cheese, whole grains, or a phosphate supplement. The results, based on serum phosphorus and urinary phosphate excretion, showed that phosphorus from meat and supplements appeared to be absorbed significantly better than phosphorus from whole grains (Karp et al, 2007).

In humans, it is thought that approximately 50% of phosphorus absorption takes place via the active transport system and half via passive diffusion. Intestinal absorption of phosphate has been found to be near normal levels in people with CKD despite the complex adaptive mechanisms present (Vervloet, 2017)

7.5. Vegetarian diets

There is some evidence that following a vegetarian diet may help to control serum phosphate levels.

In vitro studies
A small in vitro study found that a vegetarian diet rich in phytate increases the potential of the intestinal microbiota to degrade phytate (Markiewicz et al, 2013). Hence, in those following a vegetarian diet, whose intestinal microbiota have adapted to increase phytate digestion, there could be greater phosphorus absorption from phytate rich foods.

Human studies
A small crossover trial in nine patients with CKD (mean eGFR 32 ml/min) directly compared vegetarian and meat diets that contained the same amounts of protein and phosphorus. The results showed that consuming the vegetarian diet over a week resulted in significantly lower serum phosphorus levels compared with the week of consuming the meat diet (Moe et al, 2011).

A large observational cross-sectional study on 2938 participants with CKD observed lower levels of FGF23 and higher levels of serum bicarbonate among patients with CKD consuming a greater percentage of dietary protein from plant sources. Their results indicate that a diet based on plant foods may have metabolic benefits in patients with chronic kidney disease, but the safety of this dietary pattern and impact on nutritional status still need to be determined (Scalla et al, 2012).

A 4-week study on 13 subjects with CKD 3–4 examined the results of changing from a 65% animal protein diet to a 70% plant protein diet. Over the 4-week period, urine phosphorus decreased by 28% but no significant changes in serum FGF23, phosphorus or PTH were noted. There were two episodes of hyperkalemia, both corrected by food substitutions. No other adverse events were observed. The study concluded that a 70% plant protein diet is safe, tolerated, and efficacious in lowering urine phosphorus excretion (Moorthi et al, 2015).

8. Effects of food preparation – the potential to impact on phosphorus content

The phosphorus content of foods can also be modified by soaking or cooking both plant and animal foods. Several in vitro studies have been undertaken.

8.1 Reducing phosphorus in foods

The mineral content of 245 food samples pre and post processing has been analysed in a study by Jones (Jones, 1999). After prolonged soaking in water, the study showed a significant reduction in phosphorus content of the samples. The average reduction was 51% in vegetables, 48% in legumes, 38% in meat, 70% in flour and 19% in cheese. However, this procedure is likely to be poorly accepted by patients because it is time consuming and reduces the palatability and taste. There is also a potential for loss of water soluble vitamins.

Boiling is another effective method of phosphorus reduction. One small study took samples of raw beef and chicken, which were minced and then boiled. They found that minced meats which had been boiled for 10, 20 or 30 minutes removed a significant amount of phosphorus. The boiling process had a much smaller effect on protein content (Cupisti et al 2006). However, in reality it is not practical to advise patients to mince and boil meat.

8.2. Reducing phytate in plant foods

Phytate is relatively heat stable but is hydrolysed during fermentation and germination (sprouting). It also appears to be reduced by roasting, soaking and boiling. Fermentation also promotes phytate breakdown, especially in an acid medium such as in the manufacture of alcoholic drinks. Leavening of bread with yeasts (that produce phytase) also increases phosphorus bioavailability (Calvo et al, 2012)

Sprouting of seeds, grains and legumes causes phytate degradation (by up to 75%) and hence the release of phosphorus. Soaking and then roasting nuts also reduces phytate levels. Hence, some food preparation can increase phosphorus bioavailability in foods with a high phytate content.

9. The challenges faced by dietitians and individuals with CKD

Individuals undergoing dialysis treatment are recommended to consume at least 1.0-1.2 g of protein/kg ideal body weight/day which consequently increases the phosphorus load of their diets (Naylor et al, 2013). For those on dialysis, a significant amount of phosphorus is removed by this process. For example, standard haemodialysis treatment thrice weekly can remove up to 3600 mg of phosphorus (Waheed et al, 2013)

NICE recommends that the first line treatment of hyperphosphatemia should be individualised information and advice from a specialist renal dietitian (NICE, 2013). NICE also recommend the use of phosphate binding medication, if required, in addition to dietary management. These are medications that work by binding to phosphorus in the gastrointestinal tract, limiting its absorption, and can remove 200-300mg of phosphorus daily (Cupisti et al, 2013).

Phosphate binders can be taken with protein-rich foods thus helping to ensure that these foods are eaten in sufficient quantities in the diet. However, poor concordance with phosphate binding medication amongst patients with CKD is a well-documented barrier to good phosphate control for reasons such as high pill burden; difficulty in remembering to take with food; gastrointestinal intolerance; difficulty swallowing and disturbance of appetite (Nagel et al, 2014). The use of some phosphate binders may also be limited by other factors, such as the high cost of some non-calcium-based binders and the potential association of calcium-based binders with calcification of blood vessels and raised serum aluminium levels and aluminium toxicity risk with aluminium based binder usage.

As well as assessing the dietary phosphorus intake of individuals and giving advice on how to reduce the dietary phosphorus load, renal dietitians also aim to help patients achieve the most effective distribution of phosphate binding medication with the phosphorus containing foods in the diet. Secondary to the variable use of phosphorus additives by manufacturers and the potential lack of labelling declaring their use (Sherman at al 2009) phosphate binders may be ineffectively matched to dietary phosphorus intake. Phosphate binders also heavily add to the already bounteous pill burden of an individual with CKD if prescribed in sufficient numbers to block the phosphorus load of a processed diet.

10. International recommendations for dietary phosphorus intake

KDIGO states that it is important for patients to be guided toward fresh and homemade foods rather than processed foods in order to avoid additives. They also emphasise that efforts to restrict dietary phosphorus must not compromise adequate protein intake (KDIGO, 2017).

St-Jules et al (2016) recommended the following for limiting dietary phosphorus in patients on haemodialysis in the US:

- Choose commercial food items prepared without phosphorus containing food additives
- Prepare foods at home, using wet cooking methods, such as boiling (discard water)
- Substitute commonly eaten high phosphorus foods with nutritionally equivalent foods that are lower in bioavailable phosphorus.

Williams et al (2013) suggested that the role of whole grains in the diet of patients with kidney disease should be reconsidered based on their poor bioavailability and absorption.

Kalantar-Zadeh (2013) recommended the use of the phosphorus to protein ratio and stated that 'the restriction of poorly absorbed food borne organic phosphorus is unnecessary'.

11. British Dietetic Association - Renal Nutrition Group recommendations

Taking into account the information detailed in this evidence-based summary the BDA - RNG working group recommends the following dietary advice for patients with CKD who have hyperphosphataemia (Hannah et al, 2017):

1. Where possible, choose fresh rather than processed foods and prepare foods at home.
2. Ensure that dietary protein intake is adequate for the stage of CKD. Encourage fresh meat, poultry, fish, eggs, beans and pulses and a moderate intake of dairy foods to meet individual protein needs.
3. Encourage the use of wholegrain foods where possible.
4. Reduce intake of foods and drinks high in phosphorus that have low nutritional value.
5. Where possible, choose commercial foods and drinks which are prepared without the use of phosphorus containing food additives. Check the ingredient lists on food labels and reduce intake of foods containing the words phosphate or phosphoric acid. Look out for "PHOS".

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Appendix 1: RNG recommendations submitted to EFSA as part of the 2018 re-evaluation of phosphates authorised as food additives in the EU

1. Food data tables to be updated to outline the phosphorus content of additive containing and additive free foods separately.

   In order to provide evidence-based advice to our patients, we require robust data. We therefore request that the contribution of dietary phosphorus from relevant food additives is made available, as part of the planned re-evaluation of phosphates authorised as food additives.

   We were pleased to see in the 2015 Scientific Opinion on Dietary Reference Values for phosphorus that the panel recommended the development of dietary assessment tools that quantify the "phosphorus-based additives used in food processing and in some carbonated beverages" (EFSA, 2015). This research will partially address our concerns if the assessment tools are used to update the phosphorus content of foods within the food data tables.

2. Until the actual amounts of phosphorus added to foods can be quantified we recommend the phrase "Contains added phosphate" is featured on food labels.

3. Ultimately, we call for manufacturers to state on food packaging how much phosphorus has been added to the food.

   This increases patient choice as well as increasing the accuracy of assessing the phosphorus content of foods. An example of where this type of food labelling is already in place is for coeliac disease which affects only 1% of the population (Coeliac UK, 2017) and where diet is also the mainstay of treatment. However, as gluten is classed as an allergen, EU laws ensure that all food labels clearly state whether a food contains gluten to allow individuals to make easy, informed, food choices. We call for comparable ease of informed food choices to be available to the CKD community.

Appendix 2: An example phosphate additive shopping card

Look out for PHOS

E338	Phosphoric acid
E339	Sodium phosphates
E340	Potassium phosphates
E341	Calcium phosphates
E343	Magnesium phosphates
E450	Diphosphates
E451	Triphosphates
E452	Polyphosphates

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