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Review

Phytic acid: How far have we come?

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Phytic acid is a major storage form of phosphorous. Obvious reasons are there to favor its reduced concentration in organisms. However, certain justifications can also be settled, in order to support its increased natural concentration. In both cases, there are questions to be answered to favor one side while alleviating the harm of neglecting the other. This article reviews our current state of understanding of phytic acid - focusing on the topics of current and future interests in the field.

Key words: Phytic acid, phytase, myoinositol, pyrophosphate.

INTRODUCTION

Improvement in both quantity as well as quality of food is needed to cope with the increasing human pressure. Green revolution in cereals, averted problems of starvation, has helped the humanity to a greater extent but it did not address health problems related to deficiencies of vitamins and minerals. There exists a scope for improvement in quality of food (Guttieri et al., 2004). Phytic acid is widely distributed in seeds as insoluble phytin (Ca-Mg salt of phytic acid). For instance, in wheat, phytic acid accounts for 60-85% of seed total phosphorous (Raboy, 1997) and its accumulation site in the grain is aleurone layer (Khan *et al.,* 2007). Molecular formula of phytic acid is C_6H_6 [$OPO(OH)_2$] (Figure 1). In plants inositol (hexahydroxycyclohexane) is present in the form of hexaphosphate called phytic acid. Phytic acid is also termed as inositol hexaphosphate (Kasim et al., 1998), Myo-inositol 1,2,3,4,5,6 hexakis-phosphate (Guttieri et al., 2004), phytate or IP-6 (Kasim et al., 1998).

PHYTIC ACID WITHIN THE PLANT

There is a positive correlation between seed phytic acid and seed thickness. However, seed weight is negatively correlated with seed phytic acid (Khan et al., 2007). So seed thickness and seed weight can be employed as physiological markers for phytic acid content. It has been recommended that reducing the amount of phytate may render the grain minerals more bioavailable (Guttieri et al., 2004). Phytic acid can be reduced through some processing such as fermentation, breeding and perhaps through biotechnology and genetic manipulations. Now it is evident that decreasing seed-phytic-acid-content changes seed total phosphorous negligibly (Brookes et al., 2001). Efforts are underway to develop low phytic acid bread wheat for commercial production. Though, little has been achieved so far, wheat mutants with low phytic acid has been identified and reported, while different breeding programs in coordination with cereal biochemists have been structured to focus on mutants' development (Harrington et al., 2001).

There is no sustained evidence to support the hypothesis that phytin in seeds supplies energy for the processes of germination (Negvogorova and Borisova, 1967). However, it has been suggested that pyrophosphate-containing inositol phosphate compounds may serve as Pi donors for ATP synthesis. This could be potentially important during the early stages of germination prior to complete reliance on mitochondrial respiratory activity (Williams, 1970). Raboy (2003) stated that barley low phytic acid (lpa) mutants store excess P as Pi instead of IP_6. Nevertheless, seeds of lpa plants are viable and appear relatively normal, suggesting that IP_6 metabolism could not be absolutely essential for seed Pi homeostasis. Recently, Doria et al. (2009) reported a completely different storey that maize lpa-1-241 (a maize mutant defective in the synthesis of phytic acid during seed maturation) has lower germination capacity in comparison with wild type. The mutant kernels contained about 50% more free or weakly bound iron, and showed a higher content of free radicals, mainly concentrated in embryo. In addition upon accelerated ageing, the mutant seed protein were more carbonylated and DNA was more

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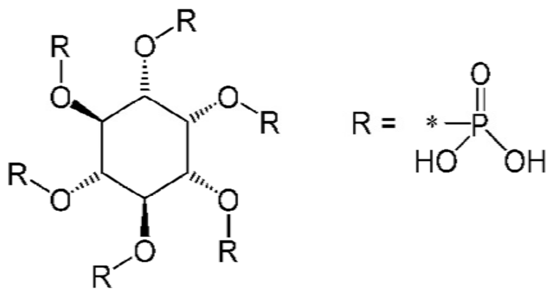

Figure 1. Structure of phytic acid, source: www.wikipedia.org/wiki/phytic_acid.

damaged, whereas, the lipids did not appear to be more peroxidated. Therefore, a novel role in plant seed physiology can be assigned to phytic acid, that is, protection against oxidative stress during the seed life span. Andiotis et al. (2005) suggested that IP6 mobili-zation is an early response of *Corylus avellana* embryonic-axes to chilling, supporting the metabolic reactivation of the dormant seeds and preparation for subsequent germination.

CHELATING AND ANTIOXIDANT PROPERTIES OF PHYTIC ACID

Phytic acid consists of a myoinositol ring with six phosphate moieties attached (Graf and Eaton, 1993). Phytic acid is believed to control blood sugar and may reduce the incidence of kidney stones. It protects against several types of cancers, for instance, breast cancer, and cancerous tumors. Fiber having phytic acid is known to be protective against colon cancer; however, it is unclear that the anti-cancerous effect is due to the fiber or the phytic acid (Jenab and Thompson, 1998). Later on, it became obvious that pure phytic acid added to low fiber diet can significantly increase the rate of apoptosis and degree of differentiation in the distal colon (Jenab and Thompson, 2000). Phytic acid also possesses properties of well known antioxidants. In contrast, phytic acid is considered to be an antinutrient because it inhibits the absorption of minerals and proteins in the intestine of the human and other non-ruminants, and thus make them indigestible (Oloffs et al., 2000; Feil, 2001). In animals, it has been associated with reduced absorption of certain minerals especially iron. Populations that depend on wheat as staple food, consume diet rich in phytic acid (Lott, 1984), bear severe consequences such as anemia, complication in pregnancy, and poor growth (Khan et al., 2007), most probably due to chelating property of phytic acid.

It acts as a natural antioxidant by chelating and reducing the catalytic activities of many divalent transition metals (Rickard and Thompson, 1997). Phytic acid is present in virtually all mammalian cells (Menniti et al., 1993) and may function as a neurotransmitter (Vallejo et al., 1988). It is a negatively charged molecule and capable of binding proteins and starches present in the diet and affect their solubility, digestibility, function and absorbtion (Rickard and Thompson, 1997) that may affect the colon environment by stimulating short chain fatty acid production from fermentation of the trapped starches (Jenab and Thompson, 1998). Also, chelating ability of phytic acid has been suggested to suppress iron-mediated oxidation in the colon, thereby reducing colon cancer risk (Shamsuddin, 1992). *In vitro* studies clearly demonstrated that phytic acid also reduce cell proliferation rate in different cell lines, including erythroleukemia (Shamsuddin et al., 1992) and human mammary cancer (Shamsuddin et al., 1996). Rimbach and Pallauf (1998) provided evidence for antioxidant properties of phytic acid under *in vitro* conditions. However, phytic acid had no significant effect on liver oxidant or antioxidant status *in vivo* in growing rats. Knowledge of the mechanisms through which phytic acid blocks angiogenesis is yet to be explored. Maybe, it blocks sprouting of new capillaries around newly forming uncontrolled cell growth by making phosphorous and other minerals less bioavailable, as angiogenesis is an energy consuming process and may only flourish if required nutrients are available. It is likely that in addition to the inhibition of iron-catalyzed oxidative damage, other pathways such as the activation of immune competent cells (Baten et al., 1989), as well as the participation of inositol phosphates in signal transduction, cell division and differentiation (Shamsuddin, 1992) are also responsible for beneficial effects of dietary phytate in cancer prevention (Rimbach and Pallauf, 1998).

PHYTASES- ENZYMES THAT DEGRADE PHYTIC ACID

The phosphate ester linkages in phytic acid are quite stable. Natural degradation is almost impossible and chemical hydrolysis in the laboratory is very slow (Turner et al., 2002). However, the enzyme phytase-found in the blood of calves, birds, reptiles and fishes (Haefner et al., 2005), in roots, vegetative storage organs and in pollen (Rayboy, 2003), in mature seeds (Williams, 1970) or secreted by variety of microbes-can rapidly breakdown phytate (Mullaney and Ullah, 2003). Phytases are hydrolases that initiate the step-wise removal of phosphate from phytate (Lei and Porres, 2003; Feng et al., 2009). Through phytate specific medium, Huang et al. (2009) isolated ten phytate degrading bacteria: *Pseudomonas* (four strains), *Brevundimonas* (two strains), *Shewanella* (one strains), *Bacillus* (one strain), *Klebsiella* (one strain) and *Citrobacter* (one strain). Phytase is strongly and competitively inhibited by Pi, while the decrease in phytase activity coincided with maximal IP6 turnover (Andriotis et al., 2005). To date, four classes of phytases have been characterized: histidine acid phosphatase (HAP), cystein phytase, purple acid phosphatase and beta-propeller phosphatase (BPP) (Lei et al., 2007). A

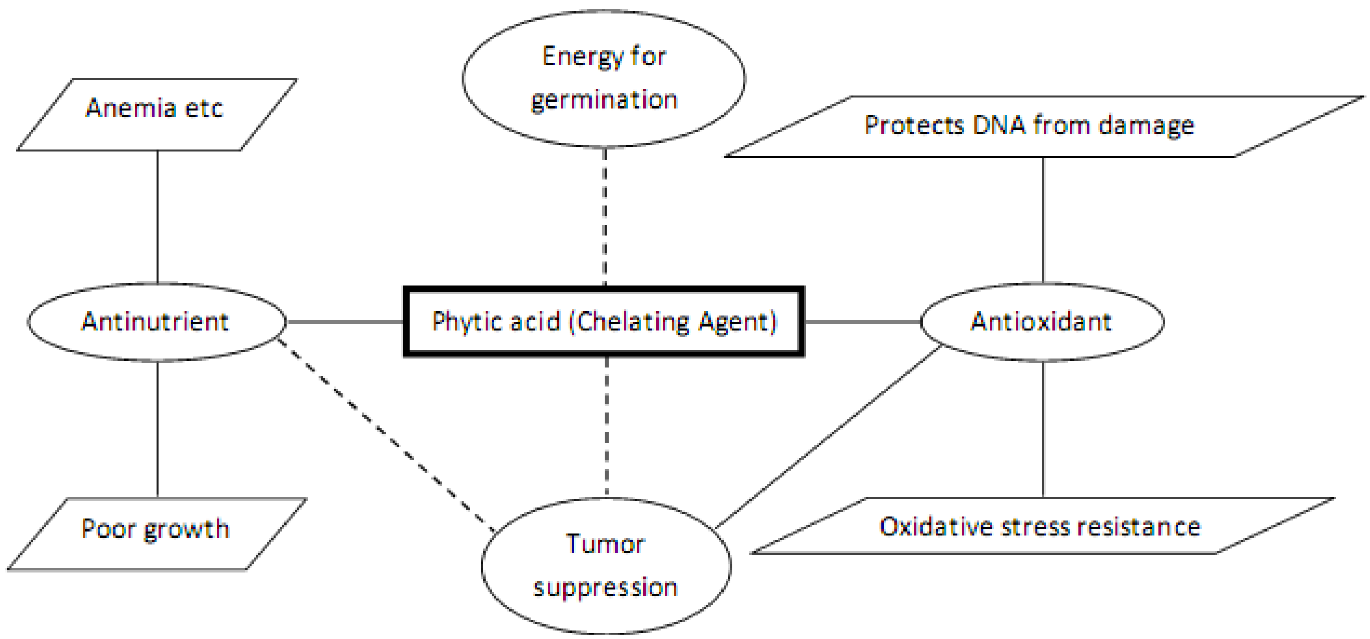

Figure 2. Model for phytic acid functions.

comparison of the properties of these phytases indicated that only BPP has a neutral optimum pH (6.0 to 7.5) for activity, whereas, the other enzymes have an acidic optimum pH (2.5 to 5.5) (Cheng and Lim, 2006). Monogastric and agastric animal do not produce intestinal phytase and thus they require phytases derived from intestinal microbes for efficient phytate hydrolysis in the neutral pH environment of intestine (Ringe et al., 1995) to facilitate optimal growth of the animals (Oh et al., 2004).

Similarly, phytases are added to animal feedstuff to reduce phosphate pollution in the environment, since monogastric animals such as pigs, poultry and fish are unable to metabolize phytate (Oh et al., 2004). Dietary phytase increases minerals bioavailability e.g. zinc bioavailability has been recently shown to be increased with dietry phytase administration to the growing pigs (Chu et al., 2009). Phytase application can reduce phosphorous excretion by up to 50%, contributing towards environmental protection (Haefner et al., 2005). While hydrolyzing phytate, HAP produces myo-inositol monophosphate as the final product, whereas, alkaline phytase produces myo-inositol triphosphate as the final product (Oh et al., 2004). A number of phytase genes and proteins have been identified from plants and microbes including bacteria, yeast and fungi. The first and probably the best characterized phytase is *Aspergillus niger* PhyA that is encoded by a 1.4 kb DNA fragment and has a molecular mass of 80 kDa, with 10 N-glycosylation sites (Lei and Porres, 2003). Expression of phytases in plants is underway to develop plant cultivars that would produce enough transgenic phytase to avoid additional supplementations to the feedstuffs (Mullaney et al., 2000).

EMERINGING INTERESTS IN INOSITOL PYROPHOSPHATES

The discovery of inositol phosphate species with seven or eight phosphates on the inositol ring was exciting and unexpected (Menniti et al., 1993). These high energy molecules have been linked to a wide range of biological functions, including vesicle trafficking, apoptosis, DNA repair, telomere maintenance and stress response (Bennett et al., 2006). Though the mechanisms of action of inositol pyrophosphates in these cellular processes remain unclear, further investigations into these fascinating signaling molecules may result in the discovery of other species, perhaps even pyrophosphorylated inositol lipids (Onnebo and Saiardi, 2007).

Model for phytic acid functions

We have proposed a model for phytic acid functions (Figure 2). Phytic acid has been known to have a role as an antinutrient, a tumor suppressor, and an antioxidant. Dotted lines show that the exact mechanisms or sustained evidence has yet to be explored.

Conclusion

With the growing scientific knowledge, phytic acid has been much explored for better outcome. However, certain questions are yet to be answered. For instance, what is the alternative sink of phosphorous in plants as there was no changes observed in phosphorous content, with the reduction in phytate, maybe there are some other less recalcitrant chelating agents that make phosphorus bound to them in plants while making phosphorous bioavailable upon digestive-enzymes-activity in human or animals. Indeed, transgenic plants for high phytase production is an attractive avenue but, here too, we need to evaluate certain unanswered questions before proceeding further, for instance, more phytase means less phytic acid remains in the animal or human body and thus it will be more exposed to cancers as phytic acid is an anti-cancerous agent. To conclude, phytic acid content should be manipulated, while managing both facets of its functions that is, chelation and anticancerous or antioxidative properties. Furthermore, signaling features of phytic acid may be explored in plants, animals and humans to trace its full expression. To sum up, this area of investigation — though carrying much interest — needs much attention and thorough evaluation to avoid complexities.

REFERENCES

Andriotis VME, Smith SB, Ross JD (2005). Phytic acid mobilization is an early response to chilling of the embryonic axes from dormant oilseed of hazel (*Corylus avellana*). J. Exp. Bot. 56(412): 537-545.

Baten A, Ullah A, Tomazic VJ, Shamsuddin AM (1989). Inositol phosphate-induced enhancement of NK cell activity correlates with tumor suppression. Carcinogenesis. 10: 1595-1598.

Bennett M, Onnebo SM, Azevedo C, Saiardi A (2006). Inositol pyrophosphates: metabolism and signaling. Cell. Mol. Life Sci. 63: 552-564.

Brookes SPJ, Lampi BJ (2001). Problems associated with measuring phytate in infant cereals. J. Agric. Food Chem. 49(2): 564-569.

Cheng C, Lim BL (2006). Beta-propeller phytases in the aquatic environment. Arch. Microbiol. 185: 1-13.

Chu GM, Komori M, Hattori R, Matsui T (2009). Dietary phytase increases the true absorption and endogenous fecal excretion of zinc in growing pigs given a corn-soybean meal based diet. Anim. Sci. J. 80(1): 46-51.

Doria L, Galleschi L, Calucci L, Pinzino C, Pilu R, Cassani E, Nielsen E (2009). Phytic acid prevents oxidative stress in seeds: evidence from a maize (*Zea mays* L.) low phytic acid mutant. J. Exp. Bot. 60(3): 967-978.

Feil B (2001). Phytic acid. J. New seeds, 3: 1-35.

Feng H, Zuo RY, Chang J, Zheng QH, Yin QQ (2009). Phytase expressed by pIAβ8 and pGAPZαA vectors and analysis of its biochemical characters. Open Biotechnol. J. 3: 19-23.

Graf E, Eaton JW (1993). Suppression of colonic cancer by dietary phytic acid. Nutr. Cancer, 19: 11-19.

Guttieri M, Dorseh BD, John A, Victor R, Souza E (2004). Identification and Characterization of a low phytic acid wheat. Crop Sci. 44(4): 418-424.

Haefner S, Knietsch A, Scholten E, Braun J, Lohscheidt M, Zelder O (2005). Biotechnological production and application of phytases. Appl. Microbiol. Biotechnol. 68: 588-597.

Harrington ME, Flynn A, Cashman KD (2001). Effects of dietary fibre extracts on calcium absorption in the rat. Food Chem. 73(3): 263-269.

Huang H, Shi P, Wang Y, Luo H, Shao N, Wang G, Yang P, Yao B (2009). Diversity of beta-propeller phytase genes in the intestinal contents of Grass Carp provides insight into the release of major phosphorous from phytate in nature. Appl. Environ. Microbiol. 75(6): 1508-1516.

Jenab M, Thompson LU (1998). The influence of phytic acid in wheat bran on early biomarkers of colon carcinogenesis. Carcinogenesis, 19(6): 1087-1092.

Jenab M, Thompson LU (2000). Phytic acid in wheat bran affects colon morphology, cell differentiation and apoptosis. Carcinogenesis, 21(8): 1547-1552.

Kasim AB, Edwards HM (1998). The analysis for inositol phosphate forms in feed ingredients. J. Sci. Food Agric. 76(1): 1-9.

Khan AJ, Ali A, Farooq-i-Azam, Zeb A (2007). Identification and isolation of low phytic acid wheat (*Triticum aestivum* L.) inbred lines / mutants. Pak. J. Bot. 39(6): 2051-2058.

Lei XG, Porres JM (2003). Phytase enzymology, application and biotechnology. Biotechnol. Lett. 25: 1787-1794.

Lei XG, Porres JM, Mullaney EJ, Pedersen H (2007). Phytase: source, structure and application. pp. 505-529. In Polaina J and MacCabe AP (ed.), Industrial enzymes: structure, function and applications. Springer, Dordrecht, The Netherland.

Lott JNA (1984). Accumulation of seed reserves of phosphorous and other minerals. In: Seed physiol. (Ed.): Murray DR. Academic Press, New York.

Menniti FS, Oliver KG, Putney JWJr, Shears SB (1993). Inositol phosphates and cell signaling: new views of $InsP_5$ and $InsP_6$. Trends Biochem. Sci. 18: 53-56.

Mullaney EJ, Ullah AH (2003). The term phytase comprises several different classes of enzymes. Biochem. Biophys. Res. Commun. 312: 179-184.

Mullaney EJ, Daly CB, Ullah AH (2000). Advances in phytase research. Adv. Appl. Microbiol. 47: 159-199.

Negvogorova LA, Borisova MN (1967). Trigger mechanism of germinating seeds. Soviet Plant Physiol. 14: 65-71.

Oh B-C, Choi W-C, Park S, Kim Y-O, Oh T-K (2004). Biochemical properties and substrate specificities of alkaline and histidine acid phytases. Appl. Microbiol. Biotechnol. 63: 362-372.

Oloffs K, Strobel E, Jeroch H (2000). Changes of phytate-phosphorus content and phytase activity in germinated feedstuffs. Bodenkultur 51(1): 41-48.

Onnebo SMN, Saiardi A (2007). Inositol pyrophosphates get the vip1 treatment. Cell, 129: 647-649.

Raboy V (1997). Accumulation and storage of phosphate and minerals. In: Cellular and molecular biology of plant seed development. (Eds.): Larkins BA and Vasil IK. Kluwer academic publishers Dordrecht, The Netherlands: pp. 441-477.

Raboy V (2003). Myo-inositol-1,2,3,4,5,6-hexakisphosphate. Phytochemistry. 64: 1033-1043.

Rickard SE, Thompson LU (1997). Interactions and biological effects of phytic acid. In Shahidi, F. (ed.) Antinutrients and phytochemical in Food. Am. Chem. Soc. Washington, DC. pp. 294-312.

Rimbach G, Pallauf J (1998). Phytic acid inhibits free radical formation *in vitro* but doesnot affect liver oxidant or antioxidant status in growing rats. J. Nutr. 128: 1950-1955.

Ringe E, Strom E, Tabachek JA (1995). Intestinal microflora of salmonids: a review. Aquacult. Res. 26: 773-789.

Shamsuddin AM (1992). Phytate and colon cancer risk. Am. J. Clin. Nutr. 55: p. 478.

Shamsuddin AM, Baten A, Lahwani ND (1992). Effect of inositol hexaphosphate on growth and differentiation in K-562 erythroleukemia cell line. Cancer Lett. 64: 195-202.

Shamsuddin AM, Yang GY, Vucenik I (1996). Novel anticancer functions of IP6: growth inhibition and differentiation of human mammary cancer cell lines *in vitro*. Anticancer Res. 16: 3287-3292.

Turner BL, Paphazy MJ, Hagarth PM, McKelvie ID (2002). Inositol phosphates in the environment. Philos. Trans. R. Soc. Lond. B. 357: 449-469.

Vallejo M, Jackson T, Lightman S, Hanley MR (1988). Occurance and extracellular actions of inositol pentakis- and hexakis-phosphate in mammalian brain. Nature, 330: 656-658.

Williams SG (1970). The role of phytic acid in the wheat grain. Plant Physiol. 45: 376-381.