

TOXINS AND THEIR MEASUREMENTS

Between the utility and hazards of phosphorus through the centuries



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Abstract

Phosphorus has been shown to be a predictor of cardiovascular mortality in kidney disease subjects. Phosphorus was discovered in 1669 and was considered a philosopher's stone, it was used as medicament but there were reported deaths after its use. High serum levels of phosphorus are associated with increased risk for cardiovascular disease in the general

population in subjects free from chronic kidney disease. Phosphorus can be defined as a useful and hazardous element for public health.

Key words: calcification, phosphorus, pollution, public health, Saint Augustine

Introduction

Phosphorus is a recognized physiologically crucial anion involved in more than one million of metabolic steps in humans and animals with a very fascinating history [1] [2]. During the Roman Empire, when the Romans used to collect large quantities of urine for industrial use, to brush teeth, to attend wounds and to whiten woolen togas; it is now known that phosphorus is an important component of detergents. Suetonius and Dio Cassius reported the method to collect the urine in Pompei: men walking in the streets of Pompei were invited to give the urine and their testicles were squeezed if they were not able to urinate [1] [2]. This was clearly painful and the men seemed to howl as do barking dogs hence the word "latrina" from "latrato" (barking). The presence of phosphorus in the nature was reported by Saint Augustine, the Christian theologian philosopher who lived from 340 to 430 AD and noted a perpetual light coming from the sepulchers of early Christians. This is now thought to be the result of the production of self-igniting phosphorus-containing gases arising from decaying bodies [3]. In the 14th century, Achid Bechil and later Teophrastus Bombastus von Hohenheim, the Swiss alchemist known as Paracelsus who lived from 1493 to 1541, mentioned that the distillation urine produced unknown substances [1]. But the clear linkage between phosphorus and urine was reported by the merchant and amateur alchemist Henning Brandt who in 1669 distilling 5500 liter of horse urine obtained 120 grams of a white substance that gave off a white light. He was impressed because he thought that the new substance was the philosopher's stone expected to turn base metals like lead in gold. The substance was named phosphorus from the ancient Greek *phos*, meaning light, and *phorus*, meaning bringing. In the following years numerous alchemists and scientists as Ambrose, Goodfrey, Kraft, Kunkel, Hensing, Gahn and Kramer studied this new substance and its properties [1] [2] [3].

Phosphorus as a medicament

In 1675 Johann Lincke, apothecary in Leipzig, was the first to sell phosphorus-containing Kunkel's pills to cure colic, asthma, fever, tetanus, apoplexy and gout [3]. Evidence of phosphorus content in the brain was described by Thomas Hensing in 1719 who suggested its relation to mental ability, and in 1730 Kramer considered phosphorus an effective remedy for epilepsy and depression [3]. In 1796, Leroy suggested the use phosphorus for the treatment of tuberculosis at a dose of 3-8 mg/day. In 1817 Annibale Omodei (Figure 1) suggested the use of phosphorus for the treatment of fever, epilepsy and paralysis but treated patients died [3]. In 1825 and in 1854 Pietro Moscati and Glover respectively examined various Galenicals used as medicaments and suggested various doses for phosphorus. In addition, Glover (Figure 2) reported a formulation of phosphorus, chloroform and cod liver to treat scrofula and tuberculosis [2]. In 1876 The British Medical Journal reported the use of phosphorus pills in British Pharmacopoeia (Figure 3) and Ashburton Thompson in his "Phosphorus in Medicine" published in 1874 considered the use of phosphorus in veneral diseases, nervous exhaustion, melancholia, softening of the brain, pneumonia, hysteria, apoplectic paralysis, impotence, migraine, epilepsy, cholera, assorted skin diseases, alcoholism, tuberculosis, amaurosis, cataract, glaucoma, tooth ache and neuralgia [3]. In 1930 a paper published in the *Journal of the American Association* recommended the use of phosphorus to stimulate the formation of new blood cells and to promote growth [1] [2] [3].

In 1935 a paper of Coltart published in *Lancet* suggested the use of phosphorus as a nerve tonic. Phosphorus was considered also as good agent to stimulate the cognitive activity [3]. [3]

Phosphorus as a hazardous element

The first real evidence of phosphorus as a hazardous element was reported by Orfila in 1817 when he

threonine kinases (Akt/protein kinase B), that are crucial regulators of cell proliferation, differentiation and metabolism [16]. It has also been reported that phosphorus is responsible for a chronic low grade of inflammation [15] [16] that could be related with telomere dysfunction via increasing ROS-mediated DNA damage and thus accelerate the accumulation of senescent cells, initiating a circulus vitiosus in which cell senescence aggravated by chronic inflammation, limits tissue regeneration and accelerates ageing [16].

Conclusion

On the basis of the previous considerations the daily intake of phosphorus exceeding 800 mg needed for the metabolic activity in humans is potentially dangerous. Many authors have suggested to reduce the daily quantity of protein originating phosphate but this can predispose to malnutrition especially in CKD patients treated conservatively or chronic

haemodialysis [8] (full text) [11]. It is mandatory to avoid foods containing polyphosphates [11][12][13][14] and beverages containing orthophosphoric acid [11] and drugs containing phosphorus [17]. Now is time to appeal to governments for interventions to abolish or limit and reconsider the use of phosphorus in dietary products. We must encourage CKD patients to adhere to phosphate binder therapy and to personalize their better hypophosphoremic therapy. Phosphorus is a useful element for the metabolic activity in humans and animals but it can become hazardous when it exceeds the serum normal range. We are convinced that it is necessary to redefine the normal range of serum phosphorus level considering the reported increased mortality risk due to cardiovascular calcifications in patients with phosphorus serum levels more than 3,5 mg/dl [18] (full text). Phosphorus has been shown to be a predictor of cardiovascular death in kidney disease subjects and in general community [19].

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