The Saudi Dental Journal 36 (2024) 1093–1096

Contents lists available at ScienceDirect

The Saudi Dental Journal

journal homepage: www.ksu.edu.sa
www.sciencedirect.com

Original Article

# Oracle of phytic acid in dental panacea – Insight into properties, therapeutic effect, regeneration, materials interaction and oral physiology

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ARTICLE INFO

*Keywords:*
Phytic acid
Regeneration
Biofilm
Inositol hexaphosphate
Restorative cements
Chelating agent

ABSTRACT

Phytic acid (inositol hexaphosphate/IP6) is a versatile chemical that is abundant in nature and is required for a variety of biological processes. It is harnessed in a wide range of fields, including drug discovery, daily supplies, chemical industries, medicine, and dentistry. IP6 is becoming increasingly popular in dentistry, with promising results. Several properties, such as cariostatic ability, beneficial impact on enamel disintegration, and anti-plaque, anti-tartar, and dental adhesive-forming properties, have been investigated thus far. Due to many constraints in the literature, there was a point in time when IP6 received less attention, which impacted knowledge in this field. Nevertheless, the positive outcomes of the flourishing of IP6 have recently been reconsidered from a number of papers that have improved our understanding of its modes of action in the aforementioned applications. The role of phytic acid in refining the properties and manoeuvring of dental resources is being investigated in novel endeavors in treating diseases of pulp and tissues supporting tooth structure, but to show its novel therapeutic potential, more precisely calibrated clinical trials are needed. This review examines and discusses the various uses proposed in the literature, as well as the applications of IP6 in dentistry.

## 1. Introduction

Phytic acid (PA) ubiquitously exists in nature as inositol phosphate (IP6) in various food grains, legumes, nuts and seeds. The literature goes back to Pfeffer's recognition of the substance in 1872. S. Posternak later labelled it "la phytine" in 1903, and Anderson published its structure in 1914. The highest concentrations of phytates were detected in plant seeds and grains, namely, wheat, soybeans, and nuts [Irvine and Schell, 2001]. They are most frequently found in nature as calcium, magnesium, and potassium salt mixtures and are also referred to as phytins. Crops and cereals with the highest phytate content supply a significant portion of inositol and phosphorous (usually accounting for 60–90 % of total phosphorous), as well as a significant cation loading site (phytate salts) and a high-energy phosphoryl group. It is also found in mammals; its concentration varies between 10 and 100 mmol/LD [Chatree et al., 2020]. On average, vegetarians consume between 2000 and 2600 mg of phytate daily. It enters the bloodstream after being swiftly absorbed in the GI tract. The large intestine of the human body also contains it biologically. The application of phytic acid for dental use is still in its infancy, with minimal research. Hence, this review was conducted to provide a sufficient background on phytic acid application in dentistry.

## 2. Properties of phytic acid

The therapeutic efficacy of IP6 has kindled the interest of scientists. IP6 has good chelation capabilities and antioxidant potential. Other functions include antiplatelet aggregation and lipid-lowering effects. IP6 suppresses human platelet aggregation in vitro in a dose-dependent manner [Vucenik et al., 2004]. In pancreatic beta cells, HIV-1 virus multiplication is inhibited, and the insulin supply is controlled. It prevents kidney stone formation by inhibiting urine calcium oxalate crystallization [Grases et al., 1998]. It is used as an implant coating for

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https://doi.org/10.1016/j.sdentj.2024.05.006
Received 29 June 2023; Received in revised form 10 May 2024; Accepted 13 May 2024
Available online 15 May 2024

magnesium alloys, which improves corrosion resistance while also stimulating new bone development. IP6 reduces the caries-preventive effect of fluoride [Cerklewski, 1992]. Nordbö and Rölla studied the ability of IP6 to prevent plaque [Nordbö and Rölla, 1972], and Cole and Bowen investigated its impact on dental plaque using rats [Cole et al. 1980]. IP6 has the ability to attach to hydroxyapatite and form a layer on the surface that prevents hydroxyapatite crystal formation and disintegration, thus preventing caries formation. In 1983, Prosser et al. developed IP6-based dental cement that had a fast setting time and was acid resistant [Prosser et al., 1983]. Recent research has investigated the potential use of IP6 in dental applications, including as a chelating agent in endodontics and an anti-staining agent in oral hygiene aids.

## 3. Therapeutic effect of IP6 in the dental domain

IP6 has recently reawakened interest in the dental field, with several research papers examining potential features such as the addition of an etchant, a chelating agent, and an anti-plaque agent to oral hygiene products.

### *3.1. Anti-cariogenic potential of IP6*

The importance of IP6 in the field of dentistry stems from its capacity to reduce the caries-preventive effects of fluoride by preventing its bioavailability from the dietary matrix when calcium is present. To increase the resistance of enamel to acid assault, IP6 can adsorb hydroxyapatite and create a monomolecular layer on the crystal surface. This layer serves as a diffusion barrier for ions, increasing the resistance of enamel to acid attack.

#### *3.1.1. Effect of phytic acid on biofilm formation*

Grases et al. reported that the use of an IP6 mouthwash reduces the amount of biofilm available [Grases et al, 2009]. This effect is associated with the ability of IP6 to modify the binding affinity of enamel as well as its capacity to prevent the crystallization of hydroxyapatite and brushite [Grases et al, 2000].

Milleman et al. analysed the effect of adding 0.85 % w/w IP6 to a tooth cream, which outperformed a control dentifrice for stain removal. IP6 is likely to be present in dentifrices both to remove stains and to inhibit the acquisition of new stains, which are assumed to be zipping to apatite crystal surfaces. By chelating with calcium, this would impair protein binding to surfaces, affecting pellicle and dye molecule adhesion as well as ionic crosslinking [Milleman et al., 2018].

#### *3.1.2. Effect on enamel crystal growth*

IP6 quickly adheres to enamel crystals, forming a coating that is only one molecule thick on the crystal surface, increasing the resistance of teeth to acidic attack by serving as an ionic dissemination barrier while also restricting hydroxyapatite development. Since IP6 is so enormous that it cannot permeate within the crystal, it mostly forms a coat on hydroxyapatite. On the crystal surface, salt complexes form and precipitate. The level of IP6 on the surface of HA remained mostly unaltered after partial disintegration or water washing, demonstrating that IP6 was compactly amalgamated to HA surfaces. Inhibiting the ability of salivary gland proteins and microorganisms to adhere to enamel by changing the properties of hydroxyapatite via the adsorption of IP6 is one way to avoid the formation of plaque [Magrill, 1973; Koutsoukos et al., 1981; Klasa et al., 2013].

### *3.2. Enriched properties of Restorative cements with IP6*

An acid-base reaction produced fast-setting cement when IP6 was introduced to the aluminosilicate glass. Due to the decreased mineral content of dentine, the resultant cement was more resistant to acid and had better adherence to the enamel. Additionally, the mechanical characteristics of zinc phosphate cements were improved by IP6. The compressive strength doubled when the IP6 concentration increased from 0 % to 2 %. The maximum compressive strength was achieved by replacing a portion of the orthophosphoric acid with 3–5 % IP6. The increased conversion of zinc phytate to zinc phosphate when some of the orthophosphoric acid was replaced with phytic acid has been used as a justification for the reduced washout of the final cement mix. This characteristic could be particularly helpful in fields such as orthodontics, where many adhesives are exposed to saliva [Li et al., 1994]. IP6 significantly slowed the hardening phase of calcium silicate-based pastes without affecting their tensile strength. [Uyanik et al., 2019].

According to Meininger et al., phytic acid was utilized as a suppressor in calcium phosphate-related cements to fulfil clinical standards for the amalgamation time of cement [Meininger et al., 2017]. The findings from an experiment by Hurle et al. [Hurle et al., 2018] on the effects of phytic acid on the hydration and kinetics of brushite cements were consistent with those of Meininger et al. It was feasible to increase the cement's injectability by forming a chelated complex between calcium ions and the phosphate groups of IP6, which had a significant delaying impact on the hydration of cement and a gradual increase in adhesive viscosity.

### *3.3. Influence of phytic acid on oral microflora*

IP6 has anti-biofilm capabilities against aerobic and anaerobic bacteria, as well as drug-resistant bacteria. Since IP6 regularly demonstrates a wide range of antimicrobial activities, it is likely that membrane film disruption serves as the main mechanism of bactericidal action. Its germicidal effect on *P. aeruginosa* and *E. coli* is mediated by disruption of the cell membrane, which increases cell permeability, modifies cell shape and decreases the intracellular ATP content. At lower concentrations, IP6 inhibited *S. aureus*, *E. coli,* and *P. aeruginosa*. IP6 has also exhibited antibiofilm efficacy against *E. faecalis* [Nassar and Nassar, 2017; Nassar et al., 2021; Nassar et al., 2023].

According to Grenby, 1967 streptococci and lactobacilli are vulnerable to IP6 acquired through the diet [Grenby, 1967]. Furthermore, IP6 has ferric chelation capabilities. Because ferrous iron is a crucial component for bacterial propagation and biofilm disposition, treatments with iron-chelating agents are effective against perilous organisms. Therefore, it is probable that the iron chelation of IP6 helps to explain its all-encompassing antibacterial and antibiofilm actions.

### *3.4. Phytic acid as a chelating and etching agent*

IP6 considerably enhanced the binding effectiveness of the resin to dentine. IP6 was found to be more efficacious than phosphoric acid and ethylenediaminetetraacetic acid (EDTA) in removing the smear layer in very small quantities, with few side effects on the dentine-pulp complex, negligible nanoleakage and mild collagen degradation [Kong et al., 2017; Forgione et al., 2021; Nassar et al., 2013]. The micro tensile bond strength increased when 1 % IP6 etchant was used to etch dentin [Nassar et al., 2021]. However, IP6 had no effect on the shear bond strength to coronal dentin [Elsayed et al., 2023]. It has been suggested that IP6 has less of an erosive effect on radicular dentin [Naeem et al., 2021; Afshan et al., 2020]. IP6 binds to demineralized and mineralized dentin in a concentration-dependent manner [Forgione et al., 2023].

Phytic acid etchant has been shown to stabilize the dentine collagen network morphology and produce enhanced resin-dentine bonding on demineralized dentine matrix either in the absence or presence of moisture [Kong et al., 2015]. IP6 can reverse the negative effects of sodium hypochlorite on dentin-resin bond strength and reduces chlorine depletion [Nassar et al., 2020]. IP6 does not alter the pulp-lysing potential of sodium hypochlorite [Chundi et al., 2022]. IP6 exhibited decreased microhardness and increased surface roughness on the dentin root canal [Muana et al., 2021].

### 3.5. Phytic acid in the Regeneration of tooth and its surrounding structures

The effects of ordinary bioactive glass and IP6-derived bioactive glass (PSC) on dental stem cells and odontoblast growth were compared by Cui et al. in 2017[Cui et al., 2017]. The formation of hydroxycarbonate apatite was increased by PSC, which could be essential for imitating an immediate connection between the biomimetic substance and the pulp dentin complex. One study reported that IP6 can trigger the release of tTGF-β and bone morphogenic protein 2 and can promote cell migration [Deniz Sungur et al., 2019; Atesci et al., 2020]. In the presence of IP6, calcium release from human periodontal ligament cells and enhanced cell viability in osteogenic media were observed [Aryal et al 2023]. The surface modification of titanium surfaces composed of phytic acid and calcium hydroxide improved bone formation and osseointegration [Liu et al., 2019; Dong et al., 2023].

### 3.6. Influence of phytic acid on the mechanical properties of dental materials

In 1980, the idea of using IP6 was proposed when it was integrated with a glass ionomer, resulting in a mixture that quickly formed due to the acid-base reaction. The mechanical properties of cements made from zinc phosphate were improved by adding IP6. With a 2 % increase in the IP6 concentration, the compressive strength quadrupled. By substituting 3–5 % IP6 for phosphoric acid, which enhanced the strength, the maximum compressive strength was obtained. When phytates were added separately, the reaction occurred quickly, the setting time was short, and the hardening time could be adjusted by changing the amount of water added or the ratio of acid to water, leading to a setting time that was more advantageous. IP6 is more stable than zinc phosphate, and it was expected that when some of the phosphoric acid was substituted with IP6, leakage from the resultant cement decreased [Li et al., 1994]. IP6 can enhance the microshear bond strength of glass ionomer cement when used as a dentin conditioner [Souparnika et al., 2023]. The above studies suggest that IP6 has substantial advantages in enhancing the mechanical properties of cements.

## 4. Conclusion

In conclusion, phytic acid is a potential natural compound in dentistry, with recent advancements in formulation and clinical testing indicating its growing relevance in oral health. Despite its potential, further research, refinement of delivery systems, and regulatory approval are essential for maximizing its benefits in improving dental care.

**Funding**.

No sources of funding were involved.

**Declaration of Generative AI and AI-assisted technologies in the writing process:**

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### CRediT authorship contribution statement

**Ummey Salma:** Conceptualization, Resources, Data curation. **C. Pushpalatha:** Conceptualization, Resources, Data curation, Supervision. **SV. Sowmya:** Visualization. **Dominic Augustine:** Visualization. **Ahmed Alamoudi:** Visualization. **Bassam Zidane:** Visualization. **Nassreen Hassan Mohammad Albar:** Visualization. **Shilpa Bhandi:** Visualization, Supervision.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgments

We thank our Librarian, Faculty of Dental Sciences, Ramaiah University of Applied Sciences for providing all the articles needed for writing this manuscript.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2024.05.006.

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