ORIGINAL RESEARCH

Arginine: A New Paradigm in Preventive Oral Care

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Abstract

Dental caries is ubiquitous and one of the most prevalent oral diseases and the foremost cause of dental pain and poor quality of life (QoL). Fluoride is an effective caries preventive agent; however, despite its use, there remain some gaps in prevention of dental caries. Arginine, an amino acid, helps to maintain a noncariogenic plaque. It shows synergistic effects with fluoride in dental caries and can help nourish the tooth by enhancing the remineralization effect of fluoride. Supplementing fluoride dentifrices with arginine can bridge the gap in caries prevention. Several clinical studies with 1.5% arginine + fluoride provide evidence for its use in prevention of dental caries. This report throws light on the benefits of arginine in dental caries and guides on its use with fluoride. Recommendations given in the report will help in effective prevention of dental caries.

Keywords: Arginine, Dental caries, Fluoride.

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Introduction

Oral health varies significantly within developing countries, with the socioeconomically deprived bearing the greatest brunt of oral disease.[1] Governments and nongovernmental agencies have focused on improving oral health in recent decades. Dental caries, commonly known as tooth decay or cavity, is one of the most common oral diseases in the world.[2] Worldwide, almost 2.4 billion people suffer from caries of permanent teeth, and 486 million children suffer from caries of the primary teeth. Indian scenario is no different from any other developed or developing country.[3]

The World Health Organization (WHO) reports that the prevalence of caries has reduced in many locations around the globe. However, the decline has been less obvious in low-income countries.[4]

A survey conducted by the Dental Council of India (DCI) in 2004 showed an increase in dental caries with age, with prevalence increasing from 51.9% in 5-year-old children to as high as 85.0% in adults between 65 and 74 years of age.[2] A systematic review and meta-analysis have shown an overall prevalence of dental caries of 54.16% in the Indian population aged between 3 and 75 years.[3]

Dental caries is a multifactorial disease with a multifaceted etiology. It is caused by acid-producing microorganisms residing on the tooth surface in the form of plaque. The microorganisms ferment sugars from the diet to organic acids, which reduces the pH below a critical level, resulting in the demineralization of the enamel. Hours after a meal, the pH of the oral cavity stabilizes until the following meal, allowing the enamel to remineralize. Disturbance between the balance of enamel demineralization and remineralization leads to dental caries.[5] Dental caries is one of the foremost causes of oral pain and the main reason patients visit dental clinics or hospitals.[2] Moreover, untreated dental caries have a detrimental effect on the quality of life (QoL). It can cause difficulties in eating and sleeping, increasing the need for invasive treatment and risk for systemic health problems shown in Figure 1.[3]

As dental caries is a dynamic process, the demineralized zone, known as early caries lesions, can be arrested and reversed by remineralization. This reversible process of dental caries is an important aspect of this condition. The other important aspect of dental caries is maintaining a balance between pathological and protective factors involved in the process (Fig. 2).[6] The pathological factors comprise acid-producing bacteria, reduced salivary function, and the frequency of consumption of fermentable carbohydrates. Saliva and its associated caries-protective elements

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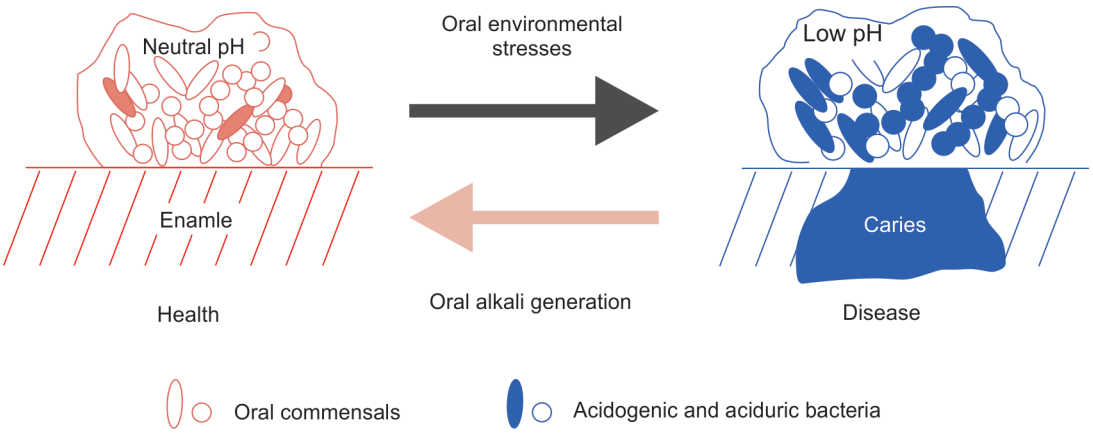
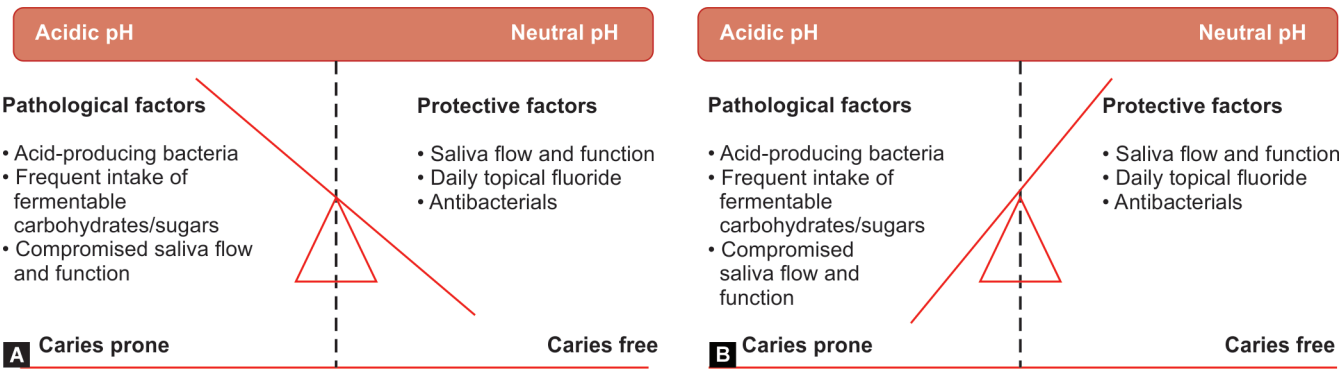


Fig. 1: Low pH leads to demineralization and dental caries[6]



Figs 2A and B: Schematic illustration of the caries balance in (A) Health and (B) Disease[7]

such as salivary flow, antibacterial, and other factors promoting remineralization are the protective factors.[7]

In health, protective factors dominate over pathological factors. In disease, pathological factors outweigh protective factors.

Optimization of protective factors enhances remineralization, shifting the balance of the caries process toward lesion arrest. A failure to alleviate the effects of the pathological factors leads to demineralization and shifts the balance toward disease initiation and progression.[8]

While managing dental caries, using noninvasive remineralizing agents at an early stage over invasive cavity restoration is preferred. Remineralizing agents encourage tooth nourishment, that is, remineralization of the already existing initial lesions and prevent further demineralization. For this, fluoride-containing agents have been the best option.[9] Fluoride is an effective caries preventive agent providing significant benefits, and the most popular topical fluoride application technique is daily brushing with fluoride-containing dentifrice.[10]

Despite the success of fluoride introduction, dental caries remains a major public health concern and an issue affecting oral health worldwide. There are several reasons behind this. Fluoridated dentifrice cannot entirely prevent the disease continuum of dental caries.[11] Fluoride does not prevent the first step in the caries process, that is, acid production by cariogenic bacteria.[12] Moreover, the actions of fluoride on acid-producing microbes may be diminishing due to the evolution of fluoride-resistant species.[9] Therefore, it is imperative to supplement fluoride dentifrice with other potent modifiers and develop new remineralization therapies to bridge the gap in caries management.[10,13]

Arginine, a naturally occurring amino acid in dietary proteins, has been introduced as an additive to fluoride dentifrice and other oral healthcare products.[10] In several clinical studies, adding arginine to oral healthcare products containing fluoride has shown to reduce the onset and progression of caries and dentin hypersensitivity.[12]

Keeping in mind the huge burden of dental caries and the additive role of arginine in preventing dental caries and enhancing tooth nourishment, an advisory board was planned to bring together experts from all over India to build a consensus regarding the role of arginine along with fluoride for combating the burden of dental caries.

Materials and Methods

An expert committee of dental practitioners reviewed the currently available data regarding arginine's role in managing dental caries. A thorough discussion and review of current evidence and their own clinical experiences formed the basis of these consensus recommendations regarding arginine's role in managing dental caries.

These expert consensus recommendations cover the following aspects:

- Burden and risk factors of dental caries.
- Role of arginine in dental caries.

The consensus was made to provide the right direction to understand and develop recommendations for arginine in managing dental caries and its prevention. The recommendation proceedings from this committee are not a substitute for clinical judgment. Adherence to these recommendations will aid clinicians and, in addition to his/her clinical judgment, create an effective treatment plan for the patient. The ultimate judgment regarding the effectiveness of any specific therapy/measure must be made

by the clinician and the patient, considering all the circumstances presented by the individual patient.

Expert Consensus Recommendations

Current Burden of Dental Caries in India *vis-à-vis* Global and Key Factors Influencing This High Prevalence

Dental caries is a chronic condition with huge variations in prevalence depending on several factors.[3] WHO data shows that the prevalence of dental caries has declined globally, but low-income countries experience a higher burden.[14] The available literature on the prevalence of dental caries in India shows that caries are quite high in certain regions and low in others. Studies including 13–19-year-olds in India report a prevalence rate of 36.7%. Apart from an overall prevalence of 54.16%, the prevalence of dental caries differs noticeably according to age, dentition, and geographical area. Age-specific prevalence was 62% in patients over 18 years and 52% in patients between the ages of 3 and 18. The mixed dentition (58%) had the highest overall prevalence of dental caries, followed by primary (54%) and permanent dentition (46%). Besides that, western India (72%) had the highest overall frequency of dental caries, followed by northern India (57%), central India (56%), and southern India (51%). Eastern India, however, showed the lowest prevalence of dental caries (36%).[3]

A person's caries risk can change as many risk factors are modifiable. Physical, biological, behavioral, environmental, and lifestyle factors that increase caries risk include excessive levels of cariogenic bacteria, insufficient salivary flow, insufficient fluoride exposure, poor oral hygiene, incorrect infant feeding methods, and poverty.[15] However, considering the changing dietary patterns in the last few decades, globalization has been associated with increased sugar consumption, contributing to the high prevalence of dental caries.[3] Based on the current evidence, it is recommended to consider the risk factors displayed in Figure 3.

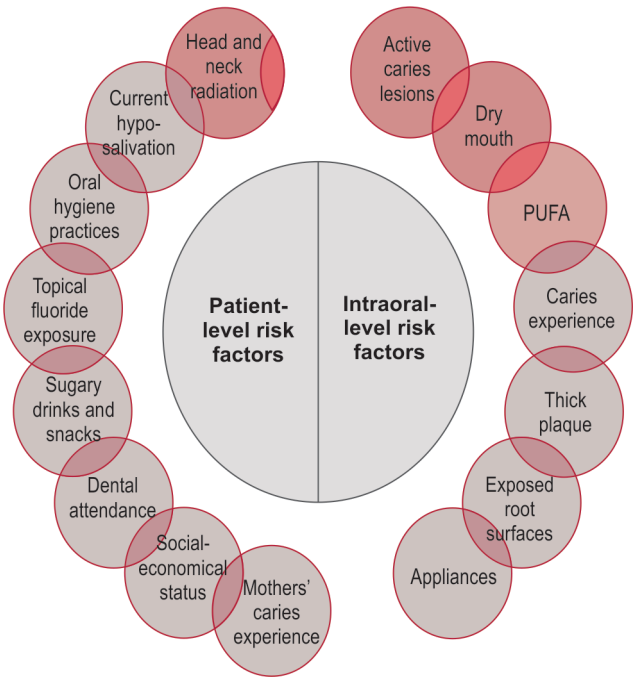


Fig. 3: Risk factors associated with development of dental caries; PUFA, polyunsaturated fatty acids[16]

Circles in red are the factors associated with a high risk of caries. The other factors can increase the risk of progression when they occur in combination or frequently. Patients' risk status should be categorized as low, medium, or high for dental caries management decisions regarding behavioral and therapeutic interventions.[16] Primary prevention approach for dental caries should be based on the common risk factors.[15] Assessment of risk factors and holistic treatment planning is important to design an effective preventive plan for caries lesions.[16]

Expert consensus on the current burden of dental caries in India *vis-à-vis* global and key factors influencing this high prevalence
• Globally, prevalence of dental caries is on the decline
• Burden of dental caries in India is higher than the global burden
• In India, there exists a remarkable variation in dental caries prevalence as per age, dentition, and geographical area
• Increased consumption of sugar contributes to high prevalence of dental caries
• A person's risk of caries can vary with time since many risk factors are changeable; hence, the assessment of risk factors is essential

Alkali Production as an Approach for Caries Control for Everyday Usage

Dental biofilms in a healthy human exhibit a balanced pH and microflora suitable for a favorable demineralization/remineralization dynamic.[17] However, these biofilms are continuously exposed to alterations in environmental conditions. The pH and source and availability of nutrients are the environmental elements that are shown to have the most impact on the composition and biochemical activity of oral biofilms and consequently on their pathogenic potential, leading to the development of dental caries. Regular consumption of dietary carbohydrates leads to acid production from bacterial glycolysis, which further induces repeated cycles of demineralization of the tooth enamel. The periods of alkalinization that occur after phases of demineralization promote remineralization and restore the enamel integrity.[18] Available evidence implies that modulating the alkali-generating potential of dental plaque may be an effective strategy to prevent dental caries.[17]

Alkali generation by bacteria of oral biofilm affects the plaque pH while preventing the occurrence of a cariogenic microflora. Hydrolysis of urea by urease enzymes and arginine metabolism *via* the arginine deiminase system (ADS) are the two primary alkali-generating routes in dental plaques (Fig. 4).[17]

The potential for alkali generation by oral bacteria to prevent dental caries is validated by several *in vitro* studies and some indirect clinical observations.[19] Data from a study that determined the relationship between ADS and urease activities with dental caries revealed significant alkali-producing potential in saliva and plaque of individuals with various caries status. A significantly higher level of ADS activity was observed in caries-free individuals than in caries-active individuals in both saliva ($p < 0.0001$) and plaque samples ($p < 0.0001$). Similarly, threefold higher urease levels were seen in caries-free subjects than caries-active subjects ($p < 0.0001$).[20]

Expert's consensus on alkali production as an approach for caries control for everyday usage

- Alkali generation from salivary substrates, like urea and arginine, may play an important role in biofilm pH homeostasis and in dental caries prevention
- The potential for alkali generation by oral bacteria as a means to prevent dental caries is supported by available evidence
- A correlation between elevated levels of free arginine in saliva and caries resistance has also been revealed

Role of Arginine in Oral Health (in the Context of Dental Caries)

- Its multifaceted mechanism of action.
- As an ecomodulator of oral biofilm and pH homeostasis *via* metabolism.
- Reversing white spots or demineralized lesions and helping to nourish by remineralizing the demineralized areas on the tooth surface.
- Synergistic action of arginine + fluoride vs fluoride alone.

Arginine is a naturally occurring amino acid found in dietary proteins, which is considered safe for use in dentifrices.[10,11] It is a major substrate for alkali generation by oral biofilms colonizing the teeth.[18] It is metabolized *via* the ADS. Arginine deaminase is the active enzyme in the ADS system, which is a surface enzyme present in oral bacteria, such as *S. sanguinis*. Arginine deaminase catalyzes the hydrolysis of l-arginine to l-citrulline, ornithine, carbon dioxide, adenosine triphosphate, and ammonia.[21] The ammonia neutralizes plaque acids and stabilizes the residual plaque biofilm on susceptible tooth surfaces. This means that arginine can prevent a shift in oral flora to aciduric bacterial species and help maintain a noncariogenic plaque.[22] Due to ammonia's effect on pH in the oral cavity, arginine and its subsequent metabolism may increase the capacity of dental plaque biofilm to produce ammonia. This may positively influence the host's ability to prevent or stop the progression of tooth decay by encouraging remineralization. At the same time, less acid is produced, reducing demineralization.[21,22] Thus, creating an alkaline environment in the oral cavity is an important advantage of arginine, as this prevents cariogenic bacteria from proliferating.[21]

A review of the scientific literature suggests that arginine improves remineralization after the addition of arginine to dentifrices.[9] The strategy combining arginine and an insoluble calcium compound, complementing and potentiating the effects of fluoride, is based on specific targeting of dental plaque, modulating its metabolism to reduce the production and effects of bacterial acid and, thereby, its pathogenicity.[22] The benefits of sodium fluoride and arginine are elaborated in Table 1.[21]

Adding arginine to fluoride-based oral products enhances the anticaries efficacy owing to their highly complementary mechanisms.[6] A cohort study by Nascimento et al. investigated the metabolic profile of supragingival plaque in response to fluoride and arginine dentifrice. Concentrations of around 16 metabolites, including agmatine, phenethylamine, and glucosamine-6-phosphate ($p < 0.05$), were significantly affected by arginine, while fluoride affected nine metabolite concentrations,

Table 1: Benefits of sodium fluoride and arginine[21]

Sodium fluoride
• Decreases hypersensitivity
• Increases remineralization
• Prevents demineralization
Arginine
• Disrupts oral biofilm
• Buffers and increases the local pH of the oral cavity
• Decreases enamel demineralization
• Increases remineralization
• Anti-inflammatory

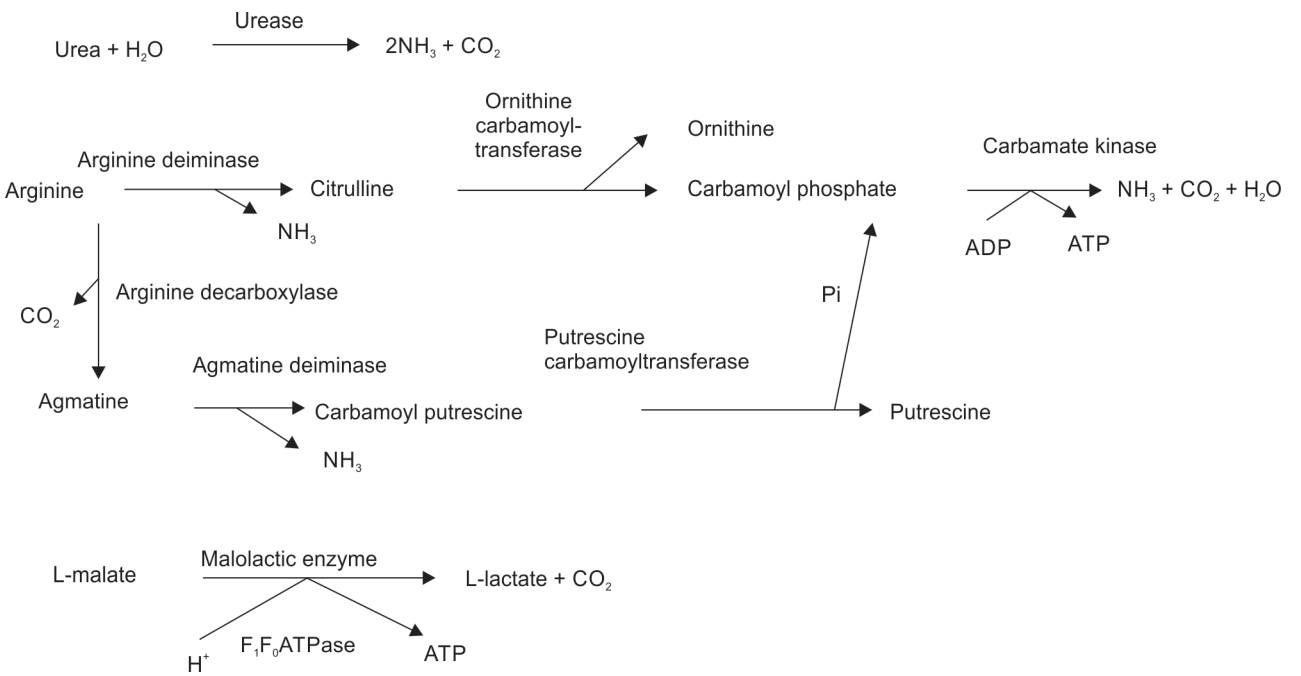


Fig. 4: Summary of alkali-generating pathways in the oral cavity[17]

including agmatine, phenethylamine, and *N*-Methyl-l-glutamic ($p < 0.05$). Fluoride enhances the resistance of tooth minerals to low pH and reduces acid production by supragingival oral biofilms, whereas arginine metabolism promotes the biofilm's pH homeostasis. Results from this study provide evidence that the mechanisms of arginine and fluoride are distinct yet complementary and/or synergistic.[23] Supplementing fluoride-containing oral products with arginine can be a promising approach to enhance remineralization and prevent dysbiosis of the biofilm related to dental caries.[24] Carda-Diéguez et al. 2022 observed a change in microbiome composition after the use of fluoride and arginine-containing dentifrice for 6 months. Use of the dentifrice was associated with an increase in common oral commensal bacteria such as *Actinomyces*, *Corynebacterium*, or *Neisseria* and a decrease in sugar-fermenting *Streptococci*. The data demonstrated a change in bacterial composition and functional profile of dental plaque toward a healthier microbial community using fluoride and arginine-containing dentifrice.[25] Results from a study by Bijle et al. 2018 showed a significant increase in remineralization of enamel caries-like lesions with 2% arginine and sodium fluoride dentifrice compared to only sodium fluoride dentifrice ($p < 0.001$).[10] Similarly, another study by Konagala et al. 2020 observed a significant rise in mineral gain (Ca + P) with arginine added to fluoride varnish compared to fluoride varnish alone ($p < 0.0001$).[9] Cheng et al. observed that arginine solution promoted remineralization compared with deionized water control ($p < 0.05$). When combined with fluoride, arginine significantly increased fluoride uptake compared with fluoride alone ($p < 0.05$). In addition, superior fluoride uptake was observed in lesions treated with arginine-containing dentifrice than those treated with conventional fluoride dentifrice ($p < 0.05$). They concluded that arginine accelerates enamel fluoride uptake when combined with fluoride, thereby enhancing enamel resistance to caries demineralization.[26]

Expert's consensus on the role of arginine in oral health and as an anticaries agent

- Arginine in combination with fluoride is a promising agent in preventing dental caries and managing incipient carious lesions
- Arginine helps production of ammonia, thereby making the environment alkaline through ADS which in turn promotes noncariogenic bacterial growth and decreases cariogenic bacterial count
- Mechanisms of action of arginine and fluoride are distinct, but they are complementary and/or synergistic
- Arginine accelerates enamel fluoride uptake when combined with fluoride, thereby contributing to the resistance of enamel to carious demineralization

Evidence Reporting the Efficacy of Arginine in Caries Prevention in Children and Adults

- Children

Can arginolysis be used as a novel and fundamental risk assessment criterion for dental caries and dental plaque?

- Adults

The management of dental caries has greatly improved over the past 20 years due to a better understanding of lesion identification methods and therapeutic approaches to arrest or reverse caries lesions.[22] The anticaries benefits of a dentifrice containing 1.5% arginine with calcium base and 1450 ppm fluoride have been demonstrated in several clinical studies conducted in adults and children.[27]

Evidence Supporting the Addition of Arginine to Reduce Dental Caries in Children

The quantitative light-induced fluorescence (QLF) method has been used in numerous clinical studies to quantify the progression and reversal of early coronal caries lesions. A 6-month randomized, double-blind controlled clinical trial by Srisilapanan et al., 2013 conducted in 331 children (7–14-years old) compared the efficacy of a dentifrice containing 1.5% arginine, an insoluble calcium compound, and 1450 ppm fluoride with 1450 ppm fluoride alone in arresting and reversing early coronal caries lesions. This study showed a significant reduction in lesion area ($p = 0.003$) and lesion volume ($p = 0.001$) with arginine-containing dentifrice compared to fluoride alone dentifrice at the 6-month examination. The study concluded that arginine dentifrice significantly improves remineralization of carious lesions.[22] Another study by Yin et al., 2013 used the QLF method to access buccal caries lesions and compared the efficacy of dentifrice containing 1.5% arginine, an insoluble calcium compound, and 1450 ppm fluoride and 1450 ppm fluoride alone in arresting and reversing buccal caries lesions. It was a 6-month randomized, controlled, double-blind clinical study conducted in 463 children (9–13-years old). The use of arginine-containing dentifrice for 6 months showed a significant reduction in lesion volume compared to fluoride-only dentifrice.[27] Both studies displayed superior efficacy of 1.5% arginine-containing dentifrice in arresting and reversing active coronal lesions and buccal caries lesions than fluoride-only dentifrice.[22,27]

Li et al. conducted a double-blind, randomized, unsupervised, parallel-group clinical trial in 6,074 school children (7–12-years old) to compare anticaries efficacy of two dentifrices containing 1.5% arginine, 1450 ppm fluoride [sodium monofluorophosphate (MFP)], and an insoluble calcium compound (either calcium carbonate or dicalcium phosphate) with dentifrice containing only 1450 ppm fluoride as sodium fluoride. Brushing with arginine-based dentifrice showed 20.5% ($p < 0.05$) and 19.6% ($p < 0.05$) reduction in incremental decayed, missing, and filled teeth (DMFT) and decayed, missing, and filled surfaces (DMFS) scores, respectively compared to fluoride only dentifrice. The study concluded that 1.5% of arginine-based dentifrices provide superior protection against caries lesion cavitation than fluoride-only dentifrice.[28]

Petersen et al. conducted a 2-year examiner blind, parallel-group, two-intervention community-based randomized controlled trial on 3,706 preschool children (4–6-years old) to assess the benefit of dentifrice containing 1.5% arginine and 1450 ppm fluoride on oral health and dental caries. Results from the study showed a 12.6% ($p = 0.005$) and 16.8% ($p = 0.001$) reduction in DMFT and DMFS scores, respectively, after 2 years, with 1.5% arginine and 1450 ppm fluoride dentifrice compared to fluoride only dentifrice.[29]

A 2-year double-blind, randomized, three-treatment controlled, parallel-group clinical study by Kraivaphan et al., conducted on 6,000 school children (6–12-years old) compared the anticaries efficacy of two dentifrices containing 1.5% arginine, an insoluble calcium compound (dicalcium phosphate or calcium carbonate) and 1450 ppm fluoride to a fluoride only dentifrice. The study showed that children using the 1.5% arginine-containing dentifrice with dicalcium phosphate and calcium carbonate for 2 years had 21%

and 17.7% fewer DMFT than children using a fluoride-only dentifrice. Similarly, 16.5% fewer DMFS were observed with both arginine-containing dentifrices compared to the fluoride-only dentifrice.[30]

Previous studies have revealed that reduced alkali-producing capacity of bacteria in the adult oral cavity is associated with a high risk for caries. Acevedo et al.[31] demonstrated that arginine-containing technology has the ability to inhibit caries in children. Production of oral alkali *via* arginine is a highly promising but understudied method for determining the risk of dental caries and preventing dental caries. Moreover, the role of arginine metabolism in oral ecology and oral health has not been thoroughly investigated in clinical studies. A study by Nascimento et al. explored the relationship between metabolism of oral arginine and dental caries in children. ADS activity was measured in oral samples from 100 children and correlated with type of dentition and caries status. It was observed that ADS activity is significantly associated with plaque caries status irrespective of age, caries status, and dentition ($p < 0.001$) of the child. Higher ADS activity was easily predicted by healthy plaque compared to diseased plaque. Substantial variations in plaque arginine metabolism among children and tooth sites were seen, which may affect their susceptibility to caries. Most importantly, findings from the study highlight that arginolysis may be a novel and fundamental risk assessment criterion for dental caries.[32]

Evidence Supporting Addition of Arginine to Reduce Dental Caries in Adults

Cantore et al. conducted a study to evaluate the effects of dentifrices containing 1.5% arginine, an insoluble calcium compound, and fluoride to promote remineralization and prevent demineralization. Addition of 1.5% arginine to dical- and calcium carbonate-based fluoride (1450 ppm) dentifrices provided greater efficacy in preventing demineralization and promoting remineralization of enamel compared to calcium base with fluoride alone.[33]

Souza et al. conducted a 6-month randomized controlled clinical study in 284 adults (30–69-years old) to compare the efficacy of 1.5% arginine, an insoluble calcium compound, and 1450 ppm fluoride as sodium MFP dentifrice with dentifrice containing 1450 ppm fluoride alone in hardening primary root caries lesions. At 6 months, it was found that 70.5% of lesions became hard in the arginine dentifrice group compared to 58.1% in fluoride alone dentifrice group ($p = 0.038$). The study concluded that 1.5% arginine-containing dentifrice has the ability to significantly arrest and reverse active root caries lesions in adults compared to fluoride alone dentifrice.[11]

Another 6-month randomized, double-blind clinical study in 444 adults (50–70-years old) by Hu assessed the ability of a dentifrice containing 1.5% arginine, an insoluble calcium compound, and 1450 ppm fluoride as sodium MFP in arresting and reversing primary root caries lesions. This study compared the efficacy of 1.5% arginine and 1450 ppm fluoride, 1450 ppm fluoride, and nonfluoride dentifrice. About 1.5% arginine-containing dentifrice showed significantly greater improvement in caries lesions at 3 months compared to nonfluoride dentifrice ($p < 0.001$) and at 6 months compared to both 1450 ppm fluoride ($p = 0.006$) and nonfluoride dentifrices ($p < 0.001$). It was concluded from the study that 1.5% arginine and 1450 ppm fluoride-containing dentifrice provide greater anticaries benefits than a conventional 1450 ppm fluoride-alone dentifrice.[34]

Experts' consensus on the efficacy of arginine in caries prevention in children and adults

- Based on the literature review, addition of arginine to fluoridated dentifrices aids in prevention of dental caries by reducing demineralization and enhancing remineralization
- The key role of arginine being the plaque modulator leads to reduction in acidogenic and aciduric bacterial counts, making dental plaque noncariogenic
- Arginolysis can be used as an adjunct tool for caries risk assessment

Interlink between Different Percentages of Arginine in Dentifrice Formulations and its Clinical Benefits

Commercially, arginine in fluoride dentifrice is available in a concentration of 1.5% and 8% arginine with 1450 ppm sodium MFP and an insoluble calcium base. About 1.5% arginine in fluoride dentifrice is introduced as a caries preventive agent, while the 8% arginine was marketed for dentin hypersensitivity.[10] A meta-analysis of results from studies by Yin et al. and Srisilapanan et al. show that addition of 1.5% arginine to fluoride dentifrice had a positive effect by showing greater reduction in the difference in fluorescence between caries and the surrounding tooth structure, indicating greater remineralization.[35]

Several studies have shown that addition of 1.5% arginine to fluoride dentifrice improved the lesion after 6-month follow-up and showed decrease in DMFT score. Evidence from the systematic review conducted by Li et al. suggests that 1.5% arginine in combination with calcium bases and fluoride dentifrice provides a superior effect compared with fluoride alone.[36]

A review on the role of arginine in caries prevention conducted by Bijle et al. included 39 articles comprising *in vitro* studies, clinical studies, and reviews. Dentifrice containing 1.5% arginine was studied in the majority of the articles. A superior anticaries effect was observed with arginine/arginine formulations compared to the matched controls including fluorides. The caries-preventive potential of arginine in commercial formulations should be explored further.[37]

Expert's consensus on the interlink between different percentages of arginine in dentifrice formulations and its clinical benefits

- As per the best available evidence, 1.5% concentration of arginine in combination with calcium bases and fluoride reported a superior effect compared with fluoride alone in patients with dental caries
- As per the available literature, no negative side effects have yet been reported following the use of dentifrices containing arginine

Evidence on the Efficacy of Arginine in Cases of Dental Hypersensitivity

Dentin hypersensitivity is a frequently encountered oral health problem affecting one or more teeth of many adult individuals worldwide. Dentin hypersensitivity arises from exposed dentin in response to stimuli, typically thermal, evaporative, tactile, osmotic, or chemical, and which cannot be attributed to any other dental defect or disease. It is characterized by a short, sharp pain that can cause severe discomfort to the patient. It impacts the eating, drinking, oral hygiene, as well as social interactions of the patient.

Various agents have been used in the management of dentin hypersensitivity, including in-office treatments and home-use-based sensitivity relief dentifrices. Many desensitizing dentifrices contain potassium salts, which cause depolarization and decrease nerve conduction. Other desensitizing agents work by occluding the dentinal tubules, leading to less movement of fluid in the dentinal tubules. Stannous or strontium-containing agents work by this method. At present, there is no gold standard treatment protocol to manage dentinal hypersensitivity.[38–40]

In 2002, Kleinberg et al. reported the development of a novel anti-sensitivity technology based on their knowledge that saliva can naturally reduce dentin hypersensitivity. Arginine, an amino acid, was the essential component of this new technology. It is positively charged at physiological pH, that is, pH 6.5–7.5. Arginine is a nonessential amino acid and has multiple functions in the body. Building blocks for collagen formation is one of the most important functions of arginine. In this technology, 8% arginine is combined with calcium carbonate, a source of calcium, and bicarbonate as pH buffer; this technology is called Pro-Argin.[41]

Arginine, in combination with calcium carbonate and phosphate, forms the positively charged glycoprotein arginine, which gets deposited on negatively charged exposed dentin surfaces. This arginine deposit helps close the open tubules and block the fluid flow mechanically, enhancing the natural process of plugging dentin tubules.[42]

Schiff et al., in 2009, conducted a double-blind clinical study to determine the efficacy of an in-office desensitizing paste containing 8% arginine and calcium carbonate relative to that of a commercially available pumice prophylaxis paste in reducing dentin hypersensitivity. Desensitizing paste containing 8% arginine and calcium carbonate provides a statistically significant reduction in dentin hypersensitivity immediately after a single professional application of the product, sustained over 28 days.[43]

Hirsiger et al. conducted a randomized control trial by using a combination of arginine prophylaxis paste and its respective dentifrice compared to a control group. The study was carried out on 273 patients for 24 weeks. The tactile and the air blast dentin hypersensitivity scores in the test group were significantly less at the end of 24 weeks than the negative control.[42]

Several other studies have shown efficacy of 8% arginine in reducing dentin hypersensitivity.[44–46] An 8th-week single-center, three-cell, double-blind, randomized study was conducted by Elias Boneta et al. to assess the efficacy of three regimens integrating dentifrice, toothbrush, and mouthwash in reducing dentin hypersensitivity. Three regimens included dentifrice containing 8% arginine and 1450 ppm MFP in a calcium carbonate base, a soft-bristle toothbrush followed by a mouthwash containing 0.8% arginine, polyvinyl methyl ether/maleic acid (PVM/MA) copolymer, pyrophosphates, and 0.05% sodium fluoride; dentifrice containing 5% potassium nitrate and 1450 ppm sodium fluoride, a soft-bristle toothbrush, followed by a mouthwash containing 0.51% potassium chloride and 230 ppm sodium fluoride; and dentifrice containing 1450 ppm MFP, a soft-bristle toothbrush followed by a fluoride/arginine-free mouthwash. The study results showed that the arginine regimen provided the greatest and the fastest reduction in tactile and air-blast dentin hypersensitivity compared to potassium and negative control regimens.[47]

A 24-week randomized, parallel-group, multicenter study was conducted to evaluate the efficacy of Pro-Argin concerning the oral health-related quality of life (OHRQoL) and cervical dentin hypersensitivity (CDH) in 273 subjects compared to a control group. The primary study parameter was a change in the OHRQoL from baseline to 24 weeks, as assessed by the Oral Health Impact Profile (OHIP)—49 questionnaire within and between the randomized groups. The mean OHIP-49 score after 24 weeks was significantly lower with Pro-Argin than with the control ($p = 0.005$).[48]

Expert consensus on the evidence on the efficacy of arginine in cases of dental hypersensitivity

- Arginine-containing pastes as a preprophylaxis paste in dental office and as long-term daily-use dentifrices have been found to be effective even after just single application
- 8% arginine with calcium carbonate has superior effects in decreasing dental hypersensitivity when compared to other desensitizing agents, such as potassium nitrate
  - Prior to oral prophylaxis with just single application
  - As a daily home use dentifrice
  - No side effects were reported in both the single-use and daily-use systems

Conclusion

Arginine, an amino acid, has been evaluated as a caries preventive agent. It has shown synergistic effects with fluoride in dental caries. Addition of arginine to fluoride dentifrices may prove to be invaluable in addressing the huge burden of dental caries as it has proven its efficacy in concentration of 1.5% for dental caries in several clinical trials in adults as well as in children. It accelerates the fluoride absorption and alters the oral biofilm. Supplementing fluoride-containing oral products with arginine can enhance its remineralization effect. Remineralization is a conservative approach for enriching teeth with minerals to prevent tooth decay. Thus, arginine can nourish the tooth by enhancing tooth enamel remineralization.

This report has been developed by a committee of experts (public health dentists, pedodontists) to understand and provide guidance regarding the role of arginine in dental caries.

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