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POTENTIAL ROLE OF L – ARGININE IN SESAME SEEDS FOR DENTAL CARIES PREVENTION

(POTENSI PERAN L – ARGININE DALAM BIJI WIJEN UNTUK PENCEGAHAN KARIES GIGI)

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ABSTRACT

Dental caries is a chronic disease caused by damage to tooth enamel. The epidemiology of the prevalence of dental caries in Indonesia is 88.80%. Some cases are detected in more severe conditions that involve pulp damage. L-arginine is one of the substances that can prevent and inhibit the progression of dental caries pathogenesis. However, few studies have discussed the role of L-arginine. This literature review aims to evaluate the potential role of L-arginine in preventing dental caries. The research uses a systematic review approach on various databases, namely PubMed, Scopus and Web of Science published in the range of 2021 – 2025. Results: After the selection, as well as the screening of articles, 5 RCT articles were found, and 4 review articles were found in accordance with the research objectives. Most studies had observational analysis outputs less 1 year so they did not show long-term results, as well as side effects of L-arginine use. L-arginine can inhibit the progression of pathogenesis of dental caries disease, as well as reduce sensitivity symptoms in the oral cavity.

Keywords: cavitas oral; cavitation; dentin caries; enamel; L-arginine

ABSTRAK

Karies gigi adalah penyakit kronis yang disebabkan oleh kerusakan enamel gigi. Epidemiologi prevalensi karies gigi di Indonesia adalah 88,80%. Beberapa kasus terdeteksi dalam kondisi yang lebih parah yang melibatkan kerusakan pulp. L-arginin adalah salah satu zat yang dapat mencegah dan menghambat perkembangan patogenesis karies gigi. Namun, beberapa penelitian telah membahas peran L-arginine. Tinjauan literatur ini bertujuan untuk mengevaluasi potensi peran L-arginin dalam pencegahan karies gigi. Penelitian menggunakan pendekatan tinjauan sistematis pada berbagai basis data, yaitu PubMed, Scopus dan Web of Science yang diterbitkan pada kisaran 2021 – 2025. Hasil*: Setelah seleksi, serta penyaringan artikel, ditemukan 5 artikel RCT, dan ditemukan 4 artikel ulasan sesuai dengan tujuan penelitian. Sebagian besar penelitian memiliki hasil analisis observasional kurang dari 1 tahun sehingga tidak menunjukkan hasil jangka panjang, serta efek samping dari penggunaan L-arginin. L-arginin dapat menghambat perkembangan patogenesis penyakit karies gigi, serta mengurangi gejala sensitivitas di rongga mulut.*

***Kata kunci** : enamel; karies dentin; karies oral; kavitasi; L-arginine*

INTRODUCTION

Dental caries, commonly known as tooth decay, is a chronic disease caused by damage to the enamel layer that can extend to the nerve part of the tooth (*pulp*).[1] A complex interaction between bacteria in the biofilm (such as *Streptococcus mutans*, *Lactobacillus*), and food residues (*primarily glucose*) causes the pH in the oral cavity to become acidic (pH < 5.5). This change is caused by the growth of bacteria that activate the glycolysis pathway, which converts glucose into lactic acid.[2] Consequently, the enamel undergoes a demineralisation process, causing the main mineral compound that makes up enamel and hydroxyapatite to degrade. If this pathogenic process continues without

intervention, the enamel structure will be damaged, exposing the dentin and pulp directly to the oral cavity.[3,4]

Enamel is formed through the process of amelogenesis and cannot regenerate itself. [5,6] Therefore, when enamel is damaged, remineralisation interventions are required to prevent the formation of enamel cavitation. *L-arginine* is an amino acid that has been widely studied for its benefits to dental health, including as a preventive therapy for dental caries.[7] *L-arginine* increases ammonia production in the mouth through metabolism by alkaline bacteria (such as *Streptococcus sanguinis*)[8]. As a result, the pH of the oral cavity returns to a neutral range (6.7–7.3), initiating the remineralisation process. L-arginine is found in seeds such as sesame, soybeans, and pumpkins. A study by Sari et al. [9] showed that the *L-arginine* extract in sesame seeds is more stable than in other seeds. However, to obtain a 100% *L-arginine* extract concentration, it is necessary to dissolve it with a proportion of 10% of the mass of sesame seeds (1013.19 mg of *L-arginine* per 1 kg of sesame seeds[9].

According to data from the Indonesian Ministry of Health,[10] the prevalence of dental caries in Indonesia reaches 88.80%, but only 57.8% of people receive dental care. Most of these individuals visit health services with complaints of tooth pain, which means the disease has been present for a long time and has caused damage to the pulp.[10] Preventing the onset of dental caries can be achieved by balancing the processes of remineralisation and demineralisation. One way to do this is by brushing teeth with toothpaste that contains active compounds such as fluoride, calcium, phosphate, xylitol, and *L-arginine*.[2] Research shows that *L-arginine* is more effective in killing cariogenic bacteria and balancing the pH of the mouth naturally. However, research and use of *L-arginine* have not been widely conducted, so this article aims to investigate the role of *L-arginine* in preventive therapy for dental caries.

METHOD

This study uses a systematic review approach on randomised control trial (RCT) articles and meta-analyses that were previously published within the period from 2021 to 2024 Literature searches were conducted across various databases, namely PubMed (n = 16), Scopus (n = 10), and Web of Science (n = 1). The keywords used in the literature search were arginine, dental caries, and sesame seeds.

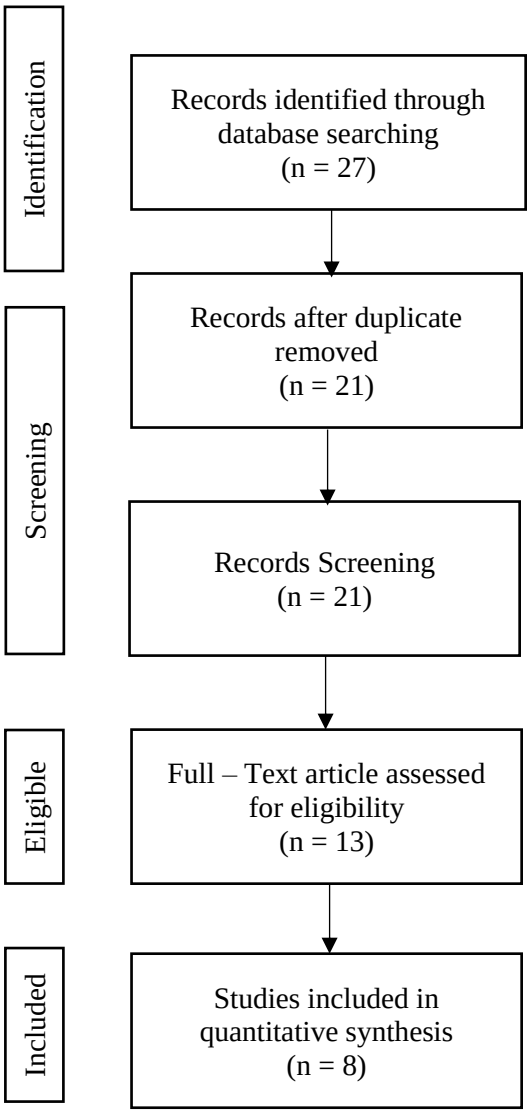

Figure 1. Searching Algorithm and Data Extraction.

A review was then conducted by reading the titles and abstracts of the articles found to eliminate duplicates or articles that did not match the theme. The authors then adjusted the articles to fit the theme and the inclusion criteria, resulting in five RCT articles and three articles discussing the theoretical role of *L-arginine* in preventing dental caries.

Randomised controlled trial (RCT) articles or reviews with the theme of the effectiveness or role of L-arginine use in preventing dental caries, involving subjects who are children or adults. Articles published between 2021 and 2025.

RESULT

A study by Razeghian-Jahromi et al.[11]discusses the growth of *S. mutans* bacteria after 24 hours. The control group was compared to the experimental group, which was given a mouthwash containing arginine. *S. mutans* is the most common bacterium responsible for forming dental biofilm and causing tooth decay. The results of this study showed that the administration of arginine at concentrations of 50–100 μM effectively reduced bacterial biofilm growth ($P<0.05$). However, at lower concentrations (< 50 μM), the control group was more effective in preventing the development of bacterial biofilm compared to the experimental group.

Table 1. The results of the study in the RCT article that was analysed with different interventions

No	Author	Result
1	(11)	The results of this study show that the administration of arginine at concentrations of 50–100 μM effectively reduced bacterial biofilm growth ($P<0.05$).
2	(12)	The data from this study indicate that the intervention group experienced a lower rate of dental caries

		progression (RRR 15.3%).
3	(13)	This study showed that after 30 days of arginine administration, there was a significant decrease in the arginine group compared to the fluoride group (P = 0.02).
4	(14)	This research found that the administration of arginine–CaCO3 effectively reduced the progression of dental caries and alleviated symptoms in patients.
5	(15)	An increase in arginine levels significantly decreased bacterial survival ($p < 0.05$).
6	(16)	High concentrations of *L-arginine* (50 and 100 μM) inhibited biofilm formation, while low concentrations (5 and 10 μM) actually increased biofilm formation.
7	(17)	*L-arginine* supplementation can reduce *S. mutans* biofilm formation without significantly inhibiting bacterial growth. Arginine also reduces the production of water-insoluble exopolysaccharides, which are essential components in the biofilm structure.

The RCT study by Pørksen et al.[12] compared 343 children (ages 5–9 years) who were given interventions with toothpaste containing arginine–fluoride and *L. casei* probiotics. The study was conducted over 10–12 months. The study sample consisted of children diagnosed with dental caries based on Ekstrand criteria (ICDAS-Lesion Activity Assessment, or ICDAS-LAA). The study compared the chronic progression of dental caries using a scoring table that included plaque stagnation area, colour, texture, cavitation, and gum bleeding. The scores were summed and classified as sound (only a colour change to brown), inactive (score = 2), and active (score ≥ 3). The results of the study (Pørksen et al., 2023) showed no significant difference between the study group and the control group ($p = 0.66$). Although not important, the data indicated that the intervention group experienced a lower progression rate (RRR 15.3%). Additional data showed that 49% of children with active caries staging decreased to sound staging after follow-up therapy. In addition, in vitro studies have shown that the combination of fluoride (2000 ppm), arginine (2%), and LGG can enhance the remineralisation process of enamel.

The study by Vaziriamj et al.[16] investigated samples from individuals aged 15–30 years who were diagnosed with dental caries. Randomisation was performed, classifying the samples into groups given fluoride toothpaste and arginine toothpaste. The results showed a

significant difference between the two groups (p-value=0.02). PCR testing for *S. mutans* levels was performed using enamel plaque and saliva samples, where the *S. mutans* count after 30 days of treatment was < 1000 in the arginine group and 35,000 in the fluoride group. The amino acid chain composition of *S. mutans* is known as GTGTTGATGCGGTGGATA.

The study by Mohammadipour et al. [14] compares the effect of a combination of arginine–CaCO3 over 3 days. The results showed a very significant difference in dental caries levels (p value=0.0002). In addition, the study showed a reduction in symptoms in patients who received therapy, including tooth pain and sensitivity to temperature (especially cold). In support of this, a study by Hafira et al. [18] evaluated the effect of adding 4% arginine to type I glass ionomer cement (GIC) used as orthodontic cementing material. The results showed that the addition of arginine significantly inhibited the growth of *Streptococcus mutans*, the primary bacterium responsible for dental caries. It indicates that arginine has potential as an antibacterial agent in the prevention of dental caries.

A study by Bijle et al.[15] aimed to assess the effect of *L-arginine* supplementation on the growth of mono-species biofilm (*Streptococcus mutans*/ *Streptococcus sanguinis*) and the underlying enamel substrate. Enamel specimens were analysed using X-ray diffraction crystallography (XRD), Raman spectroscopy (RS), and transmission electron microscopy (TEM). The study showed that an increase in arginine levels significantly reduced bacterial survival ($p < 0.05$). A survey by Nascimento et al.[19] also supported this finding, discussing the influence of arginine metabolism on the occurrence of caries in children within supragingival biofilms. The results showed that higher arginine deiminase system (ADS) activity correlated with a lower incidence of caries. It suggests that arginine metabolism may play a role in controlling the growth of cariogenic bacteria, such as *Streptococcus mutans* and enhancing the survival of non-pathogenic bacteria that are more beneficial for oral health. Furthermore, treatment with 1–2% *L-arginine* can maintain hydroxyapatite crystals, thereby preserving enamel stability and enamel biofilm homeostasis. *L-arginine* also has the potential to inhibit MMP-2 and MMP-9 through molecular docking pathways.

DISCUSSION

Anticaries Mechanism L-arginine via Arginine Deiminase Pathway

A systematic review study shows that *L-arginine* is effective in inhibiting the

progression of dental caries and protecting enamel through the activation of various pathways that alter the pH of the oral cavity to the normal range[20]. *L-arginine* is metabolised by alkaline bacteria in the mouth, such as *Streptococcus sanguinis* and *Streptococcus gordonii*, through the arginine deiminase pathway (ADP). The ADP pathway breaks down arginine into ornithine, carbon dioxide, and ammonia.[21] The ammonia compound then balances the pH in the oral cavity and activates the remineralisation process on the enamel. Remineralisation is the process of returning calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions to the enamel structure that has lost minerals due to exposure to acidic pH (< 5.5)[2]. Additionally, to support Goyal et al.'s (2023) findings regarding the remineralisation of enamel through the return of calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions, research by Wiryani et al.[22] supports the concept that enamel remineralisation can be achieved through the return of calcium and phosphate ions to the enamel structure that has lost minerals due to acidic pH exposure.

Cariogenic bacteria strongly bind (adhere) and have the ability to attach to the pellicle and start forming a biofilm (dental plaque).[2]

The role of L-arginine in Remineralisation and Enamel Protection

L-arginine can inhibit bacterial adhesion to the tooth surface. Additionally, L-arginine reduces biofilm formation by inhibiting cariogenic bacterial activity. Several previous studies also mention that patients receiving arginine therapy tend to experience a significant reduction in symptoms (e.g., tooth pain, sensitivity to cold temperatures). Abbasi et al.[23] evaluated toothpaste containing 8% arginine in 50 participants with dentin hypersensitivity, and the results showed a significant decrease in Visual Analogue Scale (VAS) scores after application and after 10 days of routine use ($p < 0.01$), indicating the effectiveness of the toothpaste in reducing sensitivity.

Moreover, *L-arginine* can balance the levels of commensal bacteria (alkaline bacteria, such as *S. sanguinis*, *Veillonella* species), as well as inhibit the growth of cariogenic bacteria, such as *Streptococcus mutans*.[2,24]

Effectiveness of L-arginine against Dentin Hypersensitivity

The combination of *L-arginine* with fluoride offers maximum protection against caries, making it a crucial innovation in modern dental care. It is because fluoride functions to reduce

hypersensitivity, enhance remineralisation, and prevent demineralisation. The combination of arginine and fluoride is considered more effective in preventing dental caries.[3]

L-arginine can be found in seeds, such as soybeans, pumpkin seeds, and sesame seeds. In soybeans and pumpkin seeds, a 5% increase in extract concentration does not increase the mass of *L-arginine*. For example, in soybeans, the 45% extract concentration has a higher mass of *L-arginine* (976.98 mg/kg) than the 50% extract concentration (848.6 mg/kg). Similarly, in pumpkin seeds, the mass of *L-arginine* is greater at the 40% extract concentration (1225.07 mg/kg) compared to the 45% extract concentration (1207.99 mg/kg), despite the percentage of L-arginine content being the same in both concentrations. These results suggest that the stability of *L-arginine* in soybean and pumpkin seed extracts tends to be lower.[9]

The study by Sari et al.[9] also shows that increasing the extract concentration by 5% in sesame seeds directly correlates with an increase in the mass of *L-arginine*, indicating better stability compared to other seeds. Additionally, sesame also contains other amino acid compounds, such as alanine, aspartic acid, cysteine, and glutamic acid.[21] In 1 kg of sesame seeds, there is 1013.19 mg of 100% *L-arginine* extract (10% of the total mass).[9]

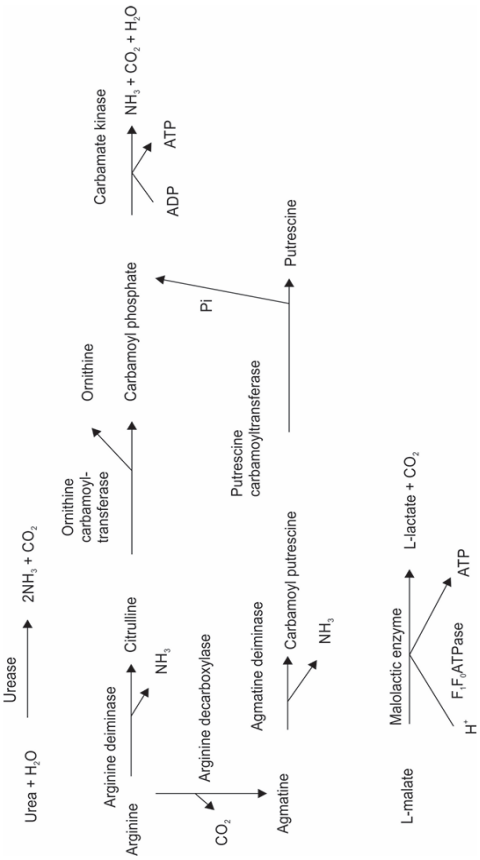

Figure 2. Alkaline Pathway Activation in the Oral Cavity.

Synergy L-arginine and Fluoride

The relationship between host microorganisms and oral cavity inhabitants is a synergistic relationship, with disbiosis often the cause of disease. In 1994, Marsh proposed an 'ecological plaque hypothesis', which underlined the importance of bacterial interaction, both with other microorganisms and host environments. It highlights the importance of collaborative metabolic activity in microbiomes and its

impact on health. Modern 'omics' and sequencing technologies have facilitated the identification of species associated with health and disease. However, the importance of every organism is the contribution it makes to the series of metabolic events that are essential to the balance of nutrients, environment, and immunology.

Modulation of microbial composition and collective metabolic activity is essential in the ecological approach to maintaining health. Therefore, the development of pro- and prebiotic solutions can be informed by assessing metabolic capabilities, which facilitate the manufacture of therapies that promote a subtle adjustment to oral microbial balance. Here, we discuss oral ecology in health and disease, focusing on metabolic changes in pro- and prebiotic treatment for caries and periodontitis.

L-Arginine stability in Natural Sources

Additionally, Kar et al. (25) compared three types of desensitising toothpaste, which contained potassium salts, natural herbal materials, and 8% arginine, in 45 patients with cervical abrasion over four weeks. The results of this study showed that toothpaste with 8% arginine provided the most significant reduction in dentin sensitivity at all time intervals ($p \leq 0.05$) compared to the other two toothpaste types. Tooth sensitivity occurs when dentin and the pulp are directly exposed to the oral cavity environment due to erosion of the enamel. *L-arginine*, together with calcium and phosphate ions from saliva, forms a protective layer over the dentinal tubules. This layer prevents stimuli from cold, hot, or sweet food from reaching the nerves in the tooth pulp.[1]

CONCLUSION

Dental caries can be prevented and its progression inhibited with the administration of *L-arginine*. Additionally, symptoms such as tooth pain and sensitivity have been reported to decrease in groups receiving *L-arginine* intervention. This study indicates that the combination of arginine and other compounds, such as fluoride, could be a significant breakthrough in the field of dentistry, especially in the prevention of dental caries.

CONFLICT OF INTEREST

This study demonstrates the effectiveness of *L-arginine* in preventing the progression of dental caries. However, there are limitations to this research, such as the limited number of articles addressing the role of *L-arginine*. Additionally, the presented observations have a short duration (< 1 year), which does not fully

reflect long-term outcomes. The study also does not discuss whether there are any long-term side effects associated with the use of *L-arginine*.

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