

## Review : Xylitol In Dental Care Formulation For Caries Prevention

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**ABSTRACT:** Xylitol is a white, odorless crystalline powder with the chemical formula  $C_5H_{15}O_5$  with chemical bonds 2R,3r,4S-Pentane-1,2,3,4,5pentehydroxypenta. Xylitol has a melting point of 92-96 °C and a boiling point of 126 °C, the density of xylitol is 1.52 g/Cm<sup>3</sup> with a mole mass of 152.15 g/mol. Xylitol has a calorific value of 2.4 calories/gram. One of the most common oral and dental diseases in the community is dental caries. Dental caries often occurs among children and adults, mostly due to not taking dental care, lifestyle, and environmental factors. The acid produced in the oral cavity is a trigger for dental caries and the process of demineralization. Another factor also stated that the occurrence of caries due to substrates of fructose, glucose, and sucrose, as well as fermented carbohydrates, could be at risk of triggering the development of caries caused by *Streptococcus mutans* bacteria. These bacteria can multiply when the contact between dental plaque and its substrate increases, while the salivary flow decreases. This journal review aims to provide information about xylitol and its relationship to caries as well as formulas for dental care preparations containing xylitol.

**KEYWORDS:** Caries, Dental, Xylitol.

### INTRODUCTION

According to research, xylitol production in the industry generally uses hemicellulose as the basic material from birch trees and corn cobs. Hemicellulose is a heterogeneous polysaccharide polymer composed of glucose, arabinose, mannose, and xylose units. This xylose will then be degraded by yeast into xylitol.



### Structure of Xylitol

Xylitol is alcohol of pentahydroxy sugars which is used as a natural sweetener in foods. Xylitol has five-carb polyol. The use of xylitol, especially in the food industry, is used as an alternative sweetener because it has a sweet taste that is equivalent to sucrose with a lower calorific value and glycemic index. Xylitol can also be used in health products such as toothpaste and mouthwash, cosmetics, and therapeutic agents in the pharmaceutical industry. Xylitol can be produced by chemical processes or by microbial processes (microbial decomposition at mild pressure and temperature and does not require very pure xylose as a carbon substrate). [5] Some microorganisms that have the ability to produce xylitol include bacteria, fungi, and yeasts.

Xylitol demand continues to increase annually by 6%. Globally, xylitol has a wide market, and demand for xylitol is in great demand in the health sector. Xylitol produced in the field of biotechnology as a sugar substitute has the potential due to its simpler steps and lower costs than chemically produced xylitol. [6] Xylitol can be extensively documented in the literature because it has a low glycemic index. Naturally, Xylitol has a very low concentration of fiber contained in vegetables, fruits, and fiber materials such as corn husks and sugarcane. [7] Xylitol has few or no side effects, has fewer calories, and is less likely to cause cavities. Xylitol also has lower cariogenicity than sucrose.

**Production of xylitol by chemical synthesis**

Xylitol can be produced chemically through the catalytic hydrogenation of xylose in a high-energy process. [8]Bioconversion of xylose to xylitol by yeast fermentation is an alternative route for the withdrawal process of chemical synthesis. [4]The chemical synthesis of xylitol from xylose is still dominant in xylitol production. [9]The process of synthesizing xylitol requires high temperatures and pressures so the process requires a lot of costs.

**Production of xylitol by microbial biosynthesis**

Xylitol biosynthesis with the use of microbes, obtained in environmentally friendly

conditions by utilizing crude sugar as a carbon source. The production of xylitol through biological routes using xylose from the hemicellulose fraction of lignocellulosic raw materials has emerged as a potential alternative way to overcome the losses experienced by the chemical route. [4]Xylose is considered to be a lower sugar when compared to glucose. [2]Xylitol production in a biotechnological process by developing recombinant strains with higher xylitol potency. [10]The xylose used is generally extracted from the hydrolyzate obtained from various sources of fruits and vegetables.

**Production of xylitol from bacteria**

Organism	Substrate	Reference
Bacillus subtilis	Xylose	[11]
Escherichia coli	Xylose	[12]
Cellulomonas cellulans	Xylose	[13]
Mycobacterium smegmatis	D-xylulose, D-manitol	[14]

**Production of xylitol from fungi**

Organism	Substrate	Reference
Aspergillusniger	D-glucose, D-Xylose	[15]
Trichoderma reesei	Xylose	[16]
Thermomyceslanuginosus SSBP	Xylose (bagasse)	[17]

**Production of xylitol from Cyanobacteria and Alga**

Organism	Substrate	Reference
Synechococcus elongatus PCC794	Xylose (straw)	[26]
Chlamydomonas reinhardtii (mengekspresikan XR dari Neurospora crassa)	Xylose (bagasse)	[27]

**Production of xylitol from yeast**

Organism	Substrate	Reference
Meyerozimguilliermondii	Xylose (bagasse)	[18]
Debaromyceshanseni UFV-170	Xylose (wheat)	[19]
Debaryomycesnepalensis NCYC 3413	Xylose (wheat)	[20]
Hansunelaanomali NCAIM Y.01499	Xylose (bagasse)	[21]

Saccharomyces cerevisiae	Xylose (wheat)	[22]
Pachysolentannophilus		[23]
Skemaffersomyces mazonensis UFMG-HMD-26.3	Xylose (straw and bagasse)	[24]
Kluyveromyces marxianus CCA510	Bagasse and cashew	[25]
Pachysolantannophilus ATTC 32691	Hemicellulose (bagasse)	[26]

### Xylitol Application

The application of xylitol in various industries has grown very rapidly, such as in the chemical industry.[28] Brazil is the world's largest fiber exporter, which accounts for 50% of total world production. About 90% of its composition is fermentable sugars such as xylose and glucose sourced from corn and bagasse. In the food industry, xylitol which has a sweet taste equivalent to sucrose is used as a sugar substitute. The nutritional value of food depends on its biological and chemical stability. The browning / Maillard reaction between reducing sugars and amino acids or proteins has an important value in the chemical stability of foods and provides a unique aroma and taste (such as in bakery products). There are some cases, such as in baby food, where the browning reaction is not recommended because it reduces the quality of the food and its nutritional value. Xylitol does not brown due to the absence of free aldehyde or ketonic groups. In addition, xylitol avoids microbial contamination because it acts as a sweetener as well as a preservative for food

products. [17]Xylitol is preferred over other sweeteners as formulations for baby food.

In the pharmaceutical industry, the biological potential of xylitol has become an interesting research topic. Consumption of xylitol can reduce plaque levels, gingival inflammation, xerostomia, and nasopharyngeal pneumonia. This can reduce microbes by several mechanisms including oxidative stress, anti-adhesive, and low permeability. [17]In the utilization of xylitol in the pharmaceutical industry, it can also be used as a mouth cleanser, dental caries, respiratory tract infections, acute otitis media, hemolytic anemia, cardiovascular, osteoporosis, lipid metabolism, anti-cancer activity, and inflammatory activity.

### Source of Xylitol

Sources of xylitol are found in a variety of fruits, vegetables, whole grains, and mushrooms. [29]There are several microorganisms including bacteria, yeast, and fungi that have the ability to produce xylitol.

Sources of xylitol	Reference
Wheat	[30]
Corn	[31]
Sugarcane	[32]
Barley	[33]
Banana, Yellow plum, strawberry, lingonberry, cranberry, bilberry, rowanberry, apple and sea buckthorn	[34]

### Dental caries

awareness of the role of oral health in improving the quality of life of infants and children at an early age in recent years has increased. The world health organization (WHO), has stated that

the prevalence of dental caries which generally occurs in children worldwide has increased. Early Childhood Caries (ECC) which is a serious health problem, active and widespread caries that often occur in primary teeth is often used as a description

of the occurrence of dental caries among children. [35] ECC causes pain, and tooth loss, and has a negative effect on the quality of life.

Dental caries is a chronic disease that is common among children. *Streptococcus mutans* is a microorganism that can cause dental caries. These microorganisms are considered humanoid carcinogens. The occurrence of dental caries due to the presence of these bacteria at a high capacity in the presence of a biofilm can be predicted by their caries susceptibility. [36] Control in dental caries aims to limit exposure to products containing sugar.

The use of xylitol can affect cariogenic bacteria that occur in children aged 6-12 years. The presence of sugar-free xylitol proves that consuming xylitol can reduce the effect on dental caries. It is known that chewing gum stimulates saliva. Supplements are useful for maintaining oral hygiene and can increase plaque pH effectively and can help reduce levels of *Streptococcus mutans* microorganisms and enamel remineralization. [36] Xylitol can limit the growth of *Streptococcus mutans* microorganisms. With the use of xylitol, plaque formation can be minimized and the amount of acid on the tooth surface can be reduced by maintaining a neutral pH in the mouth. Xylitol can also be helpful in repairing damaged tooth enamel.

According to the World Dental Federation, the most common oral and dental problem suffered by people worldwide is dental caries. Prevention of dental caries can be done in several ways, one of which is diligent brushing (twice a day) by using toothpaste that has a mechanism for preventing dental caries (such as toothpaste containing xylitol). Global data released by Oral Health Media in April 2012, as many as 60-90% of children and adults around the world almost experience dental health problems. The Ministry of Health of the Republic of Indonesia in its health research in 2018, stated that around 90.2% of children under 5 years and 88.8% of adults experienced dental caries. [37] The data also shows that people who consume national sugar per capita reach 12 kg/year.

Dental and gum disease is an important health problem in the world. Many problems concerning oral and dental health include bad breath, caries, plaque on sensitive tooth structures, and gum disease. This is due to a lack of dental cleaning. To prevent these problems, there are several things that must be done, including taking good care of oral and dental health, functional oral and dental care products that must be used

properly, and daily preventive care that must be applied. [38] The oral cavity creates favorable conditions for the reproduction of aerobic, facultative, and anaerobic microorganisms with an ambient temperature of 35-36°C, humidity, various nutrients, and varying exposure to oxygen.



**Dental caries [39]**

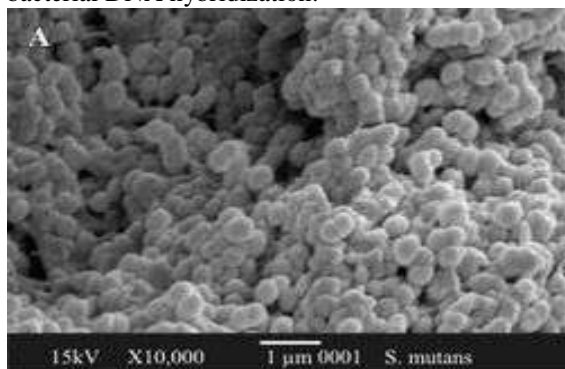
Dental caries at an early age is a complex disease that attacks children aged 3 years. Caries can be caused by damage (non-cavitory lesions or cavitory lesions). Caries often affect the primary teeth rather than the permanent teeth. This is because the dental structure of primary teeth is thinner than that of permanent teeth. [40] Dental caries can be characterized by demineralization of the inorganic part and destruction of the organic matter of the tooth, which often leads to cavity formation.

Until now, many experts have proposed various methods, measures, and means for the prevention of dental caries. [41] Xylitol can be used as an antimicrobial agent that has been used in toothpaste and mouthwash preparations to improve mechanical oral hygiene outcomes. Xylitol is a natural sugar alcohol (sugar substitute) because it has anti-cariogenic potential. The effect of increasing salivation when using xylitol-containing gum has an inhibitory effect on plaque formation. *Streptococcus mutans* is one of the main bacteria in caries formation. [41] Xylitol metabolism can reduce plaque volume, inhibit the adhesion of pathogenic microorganisms to the tooth surface, block the reproduction and acid formation of pathogenic microorganisms, and reduce *Streptococcus mutans* titers.

[42] *Streptococcus mutans* is one of the organisms in the formation of biofilms and plaque formation, due to carbohydrate fermentation. Commensal bacteria are very important for the physiology of the oral cavity, but

the formation of pathogenic microorganisms can cause serious health problems, especially biofilm infections. Actinomyces and streptococci bacteria can trigger several diseases of the oral cavity, the most common of which are dental caries, gingivitis, and periodontitis. Development of biofilm agents is an important strategy in combating oral infections. Microbial flora in the oral cavity is the most abundant microorganism compared to other areas of the body. [38] The microorganism *Streptococcus mutans* is the dominant flora present in the mouth and tooth surfaces. Biofilm formation can be controlled by brushing teeth regularly to prevent the development of dental caries and periodontal disease.

Efforts to eliminate oral pathogens in the oral cavity include the use of toothpaste, mouthwash and antibiotics which have consequential implications, and anti-biofilm therapy that is more specific and biological in improving oral health. Maintenance of a balanced microbe with the primary objective of preventing oral infections such as caries and periodontitis. Daily oral hygiene is generally for the prevention of mechanical plaque and to reduce gingivitis. [43] Dental plaque in the gingival sulcus can trigger gingivitis and promote the development of oral disease. [44][45] *Streptococcus mutans* is considered to be the main cause of dental caries because this bacterium has the ability to produce strong acids that have been isolated in saliva, plaque, and in dental cavities. [46] *Streptococcus mutans* can be classified into several groups, namely serotypes based on differences in carbohydrates in the cell wall and also based on bacterial DNA hybridization.



*Streptococcus mutans*

#### Taxonomy of *Streptococcus mutans* [46]

Kingdom :monera  
Devisio :Firmicutes  
Class :Bacili

Orde :Lacobacilalles

Family :Streptococcaceae

Genus :Sttreptococcus

Species :Streptococcus mutans

[47] Xylitol alcohol has been shown to have an impact on the growth of nasopharyngeal bacteria such as: *S. pneumoniae* and *S. mutans*, and has a role in nasopharyngeal pneumonia. [45] According to previous research, the high presence of *S. mutans* in the oral cavity, the greater the possibility of tooth decay.

#### Dental care preparations

Health problems in the oral cavity are caused by excessive consumption of sucrose and the absence of good and proper oral hygiene. [48] Prevention of this problem can be done by using antibacterial agents such as toothpaste, mouthwash, and natural sweeteners that are often used. Dental and oral hygiene treatments such as toothpaste and mouthwash, one of which contains 25% xylitol which can provide a sweet taste effectively and optimally at different concentrations in each formulation used as a complement to the preparation. Xylitol is well used as a sweetener that can prevent dental caries. Giving mouthwash containing xylitol has also been shown to significantly reduce the level of *Streptococcus mutans* bacteria in the oral cavity. [49] Xylitol with 2.2g in 20ml water can result in depletion of *Streptococcus mutans* in stimulated saliva.

#### a. Toothpaste

Toothpaste is a semi-solid product to help remove food particles, polish the surface of the teeth, freshen breath, and reduce plaque build-up. Toothpaste is a product that is popular among the public because it is considered to have a fresh effect on the mouth and is able to effectively clean teeth from dirt and bacteria that cause toothaches. Toothpaste is defined as a semi-aqueous substance that is used with a toothbrush to clean the surfaces of the teeth. [50] The use of toothpaste is one of the most widely used methods by society today, which aims to clean the oral cavity. Toothpaste contains thickeners, moisturizers, sweeteners, abrasives, foams and solvents. The materials used must be selective so that they can prevent dental and oral diseases, such as dental caries and plaque growth. Sweetener in toothpaste that acts as a commercial purpose. [3] This is the main trigger for tooth decay because it can be fermented by oral bacteria. One

of the sugars that is good for dental health is xylitol. Most toothpastes on the market use a fairly high flour. Fluorine is a substance that is useful in small amounts, but dangerous in large quantities because it can cause fluorosis of teeth. [51]The ideal properties of toothpaste are minimal abrasive effect, non-toxic, non-colouring, non-irritating, and can protect against caries and biofilm formation.

The use of toothpaste for children's dental hygiene has increased in recent years and its composition has changed a lot. At this time there have been many types of toothpaste that contain antimicrobial agents that aim to prevent and control

oral diseases associated with common microorganisms in the oral cavity. The presence of caries in children affects early childhood development. Caries can be caused by several factors, including high sugar, acid-producing bacteria, and poor oral hygiene. [44] Oral health procedures should be supervised by parents, by choosing a toothpaste that contains antimicrobial agents such as xylitol, fluoride or others, which have toothpaste components that have properties that can help children overcome dental caries. [52] Toothpaste quality requirements can be seen in the following table.

No	Parameter	Unit	Requirements
1.	pH	-	4,5 – 10,5
Metal pollutant			
2.	Pb	Ppm	Max 5,0
	Hg		Max 0,02
	As		Max 2,0
Microbes			
3.	Total Plate count	-	<10 <sup>5</sup>
	E. coli	-	Negative
6.	Organoleptic	-	Must be homogeneous, with no visible air bubbles, no lumps, and no separate particles.

[53] Toothpaste formulas contain basic ingredients, including:

- **Abrasive material:** which serves to clean and polish (polish) teeth, generally based on lime or silica.
- **Detergent:** detergent foam can remove plaque and other debris from the tooth surface. ex: sodium lauryl sulfate
- **Binder:** serves to separate solid and liquid materials during storage. For example: cellulose and the most commonly used is sodium carboxy methyl cellulose.
- **Humectants:** to retain moisture and prevent toothpaste from hardening when exposed to air. Generally use glycerol, sorbitol and

propylenglycol, which gives toothpaste its sweet taste.

- **Flavors, sweeteners, fragrances:** peppermint, spearmint, cinnamon, wintergreen and menthol which are ingredients that are widely used for refreshing or flavoring.
- **Preservatives:** Alcohol, benzoate, formaldehyde and dichlorinated phenols which are used to prevent the growth of bacteria in humectants.
- **Xylitol and fluoride** as therapeutic agents, generally as caries prevention agents with other ingredients to control plaque, tartar and gingival abnormalities

Formulation	Treatment	Content of agent	Reference
Xylitol Na.saccharin Na.Lauryl Sulfate Sorbitol Propylene glycol flavoring	Xylitol in the formulation with a concentration of 5% is able to provide an enamel remineralization effect	Xylitol 5%	[54]

agent			
Na.carboxymethyl cellulose Na.Fluoride Xylitol Sorbitol Glycerin Strawberry Flavor	The use of xylitol 10% combined with 0.24% fluoride, both have the same effect (can decrease salivary pH).	Xylitol 10% Fluoride 0,24%	[41]
Xylitol Fluoride	Xylitol which is anticariogenic has antibacterial and antiplaque effects.Xylitol combined with fluoride can reduce the occurrence of dental caries.	Xylitol 10%- No Fluoride	[55]
Xylitol Fluoride	Xylitol and fluoride can reduce the level of Streptococcus mutans bacteria in saliva concentrations.	-	[56]

[54]In a study conducted by that the addition of 5% xylitol has a good effect on the effect of increasing remineralization so that xylitol is good to use because of its ability to inhibit the risk of dental caries. In the second study, with 10% xylitol concentration combined with 0.24% fluoride, the results obtained both had the same effect, which was to lower the salivary pH. Saliva is rich in calcium produced and saturated phosphate, so at an alkaline pH, saliva can neutralize the acid that occurs due to plaque bacteria. [41]The more alkaline the pH of the saliva produced, the more remineralization on the tooth surface in the presence of bicarbonate ion deposition. [55]In a study explained that xylitol and fluoride were effective in caries inhibition. Both exhibit anticariogenic effects. [56]The fourth formulation based on research the use of this combination can affect the amount of plaque. Xylitol is used as an effective sugar substitute which can function to reduce the number of Streptococcus mutans bacteria in saliva so as to get the maximum effect.

**b. Mouthwash**

[57]Mouthwash is used to control dental plaque, done mechanically by brushing the teeth or interdental. [57]According to research. to mechanically control plaque can also use mouthwash, this is done to control the achievement of areas that are not reachable by tooth brushing. Mouthwash that is used as an oral cleanser functions as a deterrent to microorganisms adhering to the pellicle or tooth surface and acts as a bacteriostatic agent. Mouthwash that is used long-term is not safe to use because of its very wide use and can also cause resistance to various types of antibiotics that function to inhibit oral mycobacteria effectively. [58]In short-term use, mouthwash is effective in wound healing, periodontitis, gingivitis and canker sores. [59]Mouthwash is used to rinse your mouth after brushing or flossing your teeth, it serves to maintain dental hygiene and protect against tooth decay.

Ingredients	Content of xylitol	Xylitol function	Effect of xylitol	Reference
Pineapple peel extract Glycerin Benzoic Acid Xylitol Oleum menthe Aquadest	10 %	Additional sweetener combined with glycerin	Functions as a preventative from dental plaque and is non-cariogenic	[60]
Glycerin Xylitol Peppermint and lemon flavor GTE Plum Extract	5 %	Sweetener	Xylitol used as an inhibitor of Streptococcus mutans	[61]

Areca seed extract Glycerin Menthol Propylene glycol Xylitol Aquadest	3 %	Sweetener and antimicrobial	Inhibits the growth of Streptococcus mutans	[62]
Sodium florida Sodium benzoate Xylitol Saccharin Sodium Menthol Methyl paraben Essential oil of B. dracunculifolia Mint Hydroethanol extract of B.dracunculifolia Sorbitol PEG 40 Glycerin Pure water	2,50 %	Sweetener	Xylitol which contributes as a sweetener that aims to reduce the occurrence of plaque on the tooth surface.	[63]

The first formulation carried out by stated that the addition of xylitol sweetener in the formulation with a concentration of 10% combined with glycerin could mask the chelating taste and give a sweet taste. Xylitol functions as a preventer of dental plaque and is non-cariogenic. [61]The second formulation was research conducted by .that xylitol was used as an effective sweetener in inhibiting the growth of Streptococcus mutans bacteria in the oral cavity. [61]The composition of saliva when using mouthwash can reduce the level of organic acids in the oral cavity. [62]The third formulation showed that the mouthwash of areca nut extract formulated with xylitol as the base material functions as an antimicrobial agent and sweetener, which can affect the occurrence of Streptococcus mutans bacteria inhibition. [63]In the fourth formulation, that the use of xylitol as a sweetener contributes to reducing plaque on the tooth surface that occurs due to the presence of microorganisms in the oral cavity. [63]Xylitol is able to reduce the production of acid in the oral cavity. Mouthwash made from natural and commercial ingredients can reduce the occurrence of plaque, prevent biofilm, and reduce the occurrence of dental caries.

#### Xylitol Dosage

[64]The use of xylitol in preventing caries has several important parameters including dose, frequency of administration, and saliva

concentration. 5 g of xylitol can be divided into 3 times a day in achieving the prevention of dental caries. The effectiveness of using xylitol depends on the dose, frequency, and duration of its use. [65]Using a dose of xylitol as much as 3.4gr / day showed significant results in terms of inhibiting the development of caries and plaque buildup. The use of high doses of xylitol in adults and children can cause gastrointestinal effects that can be detrimental. [64]The intake of xylitol used in adults is around 200g/day while in children it is 45/day. [66]According to the study of Cardoso et.al, the effective dose of xylitol is in the range of 6-10g/day. Based on the data indicated that suppression of Streptococcus mutans would require the consumption of about 2g of xylitol per day, with a polyol concentration of 0.5% - 65%.

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