Demineralization – An Overview of the Mechanism and Causative Agents

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Abstract

Various tissues in the body like bone, enamel dentin and cementum are composed of inorganic material and they are exposed to multiple cycles of Demineralisation and remineralisation. Understanding these biological mechanisms are necessary for developing treatments for these mineralisation related diseases and specifically dental caries as far as dentistry is concerned. This article focuses on the mechanism and rate of demineralisation and discusses in detail the causes of demineralisation.

Keywords: *Demineralization, dental caries, pH, remineralization.*

Introduction

Enamel, dentin, and cementum are made of inorganic crystals embedded within their organic matrices. [1] Demineralisation is the process of removing mineral ions from the dental hard tissues resulting in the loss of structural integrity. Demineralisation refers to dissolution of enamel and is usually the first step to the formation of dental caries. However, cycles of demineralisation are alternated by cycles of remineralisation where protective factors promote remineralisation and pathological factors shift the equilibrium towards cavitation. Various factors like pH, salivary flow, mineral content, degree of dissociation, microbial flora and diet affect the demineralisation-remineralisation balance.[2]

Mechanism and Rate of Demineralisation:

Dentin forms the bulk portion of teeth with 70% inorganic substance, 20% organic substance and 10% water. The inorganic matrix is mainly hydroxyapatite crystals that are embedded within the organic material. There is a hypothesis that states organic matrix is made of type I collagen that acts a protective sheath over the crystals.[2]

A unit mass of solid hydroxyapatite dissolves five calcium ions, three trivalent phosphate ions and one hydroxyl ion that are released into solution.

$$Ca_5 (PO_4)_3 OH \text{ « } 5 Ca^{2+} + 3PO_4^{3-} + OH^-$$

The extent to which tooth mineral can dissolve in a solution is determined by ionic product of calcium, phosphate, and hydroxyl ions. The product of soluble ions of a salt in a solution is called ion activity product (IAP)

$$(IAP)_{HA} = (Ca^{2+})^5 X (PO_4^{3-})^3 X \text{ OH -}$$

IAP = (KSP) HA solubility product of hydroxyapatite = constant — 7.41 x 10 mol 9/19 - saturation — equilibrium.

IAP > KSP (the solution is supersaturated with tooth mineral ions) induce formation of HA crystal growth.

IAP<KSP (the solution is under-saturated)- dissolves HA (hydroxyapatite) demineralization. At neutral pH, saliva and plaque fluid are supersaturated with HA, prevents enamel from dissolution, causes precipitation of calcium phosphate brushite CaHPO,2H,0, not HA.[3]

Formation of pellicle on the enamel surface inhibits precipitation of calcium phosphate from supersaturated saliva. The micro radiographic analysis showed that after 4 to 8 weeks of in situ demineralisation, the lesion depth values were 33±12 and 63±17 μu, respectively. It was concluded that the lesion depth as well as the mineral

loss parameter both vary linearly with demineralisation time. [4] According to a study done in 2019 by Meng Tsan Tsai, using OCT (Optic coherence topography) to characterize the acid effect on enamel, it was noted that the surface roughness and scattering coefficient increased significantly after acid exposure. [5]

N Sabel et al in 2012, stated that the rate of demineralisation varies considerably with the chemical composition of the enamel. Higher the carbon content, the demineralised lesions were deeper. Also, depth of the lesion increased if the degree of porosity in the enamel was higher. [6] Oki Hayah et al. in 2016, compared the demineralisation depths of teeth in two different age groups (20s and 60s). It was concluded that demineralization depth increased with time and there were no significant differences in demineralization depth between the two age groups. [7]

Effect of Ph On Demineralization:

According to the law of saturation, a dynamic equilibrium exists between oral fluids and minerals. pH is one of the most important factor that determines the extent of enamel demineralisation and demineralisation. Critical pH is the point at which the solution becomes 'just' saturated with the minerals or the pH at which saliva is saturated with HA.[8]

The solubility of HA is affected by the pH of water. At alkaline pH 14, phosphates are in the ionic form PO_4^{3-}. As the pH is lowered PO_4 & OH accumulate in solution, together with calcium ions and dissolution of HA slows as the solution becomes saturated. In acidic pH, PO_4^3 (phosphate) & OH ions combine with H^+ to form HPO_4^{2-} (hydrogen phosphate) and H_2O respectively removing a portion of phosphate and hydroxyl ions from the solution. As this transformation of ionic phosphate takes place, saliva ceases to be saturated with HA, solubility of calcium phosphate increases as the pH decreases. [9] Alkaline pH is 7.2- 12.3 and acidic pH ranges from 2.1-7.2 and the critical Ph for HA= 5.3-5.5. Below the critical pH enamel demineralises and above critical pH enamel remineralises. Post radiation the pH lowers from 7 to 5 which is cariogenic. As a result, the buffer is not maintained resulting in the dissolution of enamel minerals. [10]

Fluorapatite crystals and enamel demineralisation:

Enamel is a crystalline structure consisting of hydroxyapatite crystals and when the fluoride ions substitute the HA, it becomes fluorapatite or hydroxy fluorapatite. The critical pH for fluorapatite is 4.5. Therefore, the enamel has better stability and hardness in low pH when HA crystals are replaced by fluoride ions.[11,12] Fracture toughness, modulus of elasticity and hardness is better with fluorapatite when compared with hydroxy fluorapatite crystals of different proportions of fluoride and hydroxyl ions [13] The decrease in solubility and superior biological properties was noted in samples with increase fluoride content when ion release was compared between samples containing different ratios of HA, fluorapatite and hydroxy fluorapatite ions to pure water. [14]

Causes of Demineralisation:

Saliva:

Saliva is composed of various proteins like statherin, albumin, histatins, cysteines and various ions like calcium, phosphates and fluorine ions. The composition, pH, antibacterial activity, the quantity and viscosity of saliva flow has profound effect on the rate of demineralization. [15] Albumin accounts for more than 50% of all serum proteins, present as serum ultrafiltrate, it penetrates through the enamel pores and forms a protective barrier against enamel demineralisation. [16] Mithra Hegde et al., in 2017, concluded that calcium loss was less in enamel samples coated with albumin in comparison to samples that were not coated with albumin demonstrating that albumin is a strong protective barrier against enamel demineralization. Salivary proteins' ionic concentration is mainly made up of calcium and phosphates which determines the rate of mineral loss. Salivary flow decreases in Sjogren's syndrome, sarcoidosis, radiation therapy and diabetes. The viscosity increases and the quantity decreases which considerably alters the salivary buffering capacity and the oral microflora resulting in increased susceptibility to caries. [17]

Dental Plaque:

Dental plaque is defined as a gelatinous mass of

bacterial biofilm adhering to the tooth surface. When the specific hypothesis failed as it was impossible to eliminate/ isolate the specific plaque bacteria that was pathogenic, a new concept called the 'ecological plaque hypothesis' was proposed. According to which, an environmental change can provide pathogenicity to the residing microbiota at specific sites and hence disease is caused only at certain sites.The plaque microorganisms are usually Streptococcus, lactobacillus and actinomycetes which metabolize the refined carbohydrates producing acids as the by-product. This lowers the pH at the plaque enamel interface. When pH is below the critical point, it results in enamel demineralisation. When oral hygiene is poor, the thick plaque prevents salivary buffering action on enamel resulting in demineralisation.[18]According to Zhang Y et al., 2000, it was concluded that when enamel was exposed to lactic acid with similar degree of saturation of plaque fluid, demineralisation and mineral loss increased significantly as the degree of saturation dropped. [19]

Role of diet in enamel demineralisation:

During an acidic attack there is dissolution of inorganic matter and the destruction of the organic matrix. Teeth is exposed to acids during bacterial fermentation.Streptococcus species and lactobacillus are aciduric being the main culprits. Organic acids like lactic acid produced during the process of fermentation considerably lowers the pH resulting in demineralisation while producing indigestible extra cellular dextran from dietary sugars which promotes bacterial colonisation. The frequency of consuming free sugars should be limited to less than 4 times a day. Dietary soda includes citric acid and phosphoric acid that causes demineralisation resulting in caries or enamel erosion. Also, fibrous diet rich in calcium and phosphorous causes remineralisation by preventing the pH falling below 5.5. [20]

T R Razvan et al., in 2016 evaluated the enamel demineralization depth by five sweeteners. Currently, five sweeteners have been approved by Federal Drug Administration which are Aspartame, Saccharine, acesulfame, sucralose and neotame. The most investigated artificial sweetener is sucralose, a non-caloric sweetener. Recent studies have demonstrated that manuka honey with a high antimicrobial activity is said to be non-cariogenic. The depth of demineralisation on consumption of various sugars was as follows : Palm sugar (196.07µm), Sucralose (145.47µm), Glucose (235.72µm),Sucrose (287.78µm) and honey (160.01µm) Therefore, the lowest depth of demineralization was observed in sucralose followed by honey.[21]The highest depth was observed in sucrose. Oral hygiene maintenance combined with consumption of the right diet is important in prevention of dental caries.

Acid etching:

Acid etching technique is defined as the process of roughening a solid surface by exposing it to an acid and thoroughly rinsing the residue to promote micromechanical bonding of an adhesive to the surface in other words dissolution of HA crystals to create micro porosities for bonding. Enamel topography changes from a low reactive surface to a surface favouring adhesion and bonding. Generally, total etch technique involves the use of phosphoric acid (37 %) with an etching time of 15 sec, rinsing time of 30 secs to achieve the most receptive enamel surface for bonding. Demineralisation due to acid etching can be selective as the morphology of prisms varies from region to region. It can either be in the prism head or at the periphery which are type I and type II etching patterns, respectively. Etching can remove up to 10 micrometres of enamel. A properly etched surface gives a frosty white appearance on drying. Micro tags are the finer particles of numerous small tags (resin tags) formed across the end of each rod where the individual hydroxyapatite crystals are dissolved. Demineralization paves the way for the formation of resin tags and the hybrid layer, forming the fundamental basis of adhesion to dentin.

IAP<KSP (the solution is undersaturated)- dissolves HA demineralization. This is of paramount importance for a favourable clinical performance of composite resin restorations' adequate adhesion.[22]However, when acid etching is prolonged, it can have dramatic effects of the properties of enamel. In a study by Zafer et al. 2015, enamel was treated with 37% phosphoric acid at varying time duration. It was concluded that etching time can have profound effects on surface properties of enamel such as increase surface roughness and decrease surface hardness which in turn can affect the bond strength and longevity of composite restoration.[23]

Dental caries and demineralisation:

Dental caries involves a sequalae of multiple processes- complex interaction between the microbial film, tooth structure and diet. During demineralization, the HA crystals are dissolved first, exposing the collagen to dissolution. In the dental fraternity, diagnosis of dental caries means identifying the demineralised regions and restoring it with various dental cements or other appropriate treatment options. Demineralisation in its initial stages is identified with an electron microscope and after several stages becomes a white spot lesion which then progresses into cavitation. This can be detected visually and radiographically. Carbon content plays a key role in deciding the rate of demineralisation. The carbonate ion substitutes the phosphate ion produces defects in calcium deficit areas. In enamel one out of ten phosphate ions are replaced with carbon and in dentin one out of five. Therefore, the minerals loss in dentin is three times greater than enamel, due to high carbonate content. [24]

Caries of enamel has revealed four distinct zones starting from the advancing front of the lesion. First is the *translucent zone* -being the advancing front of caries. The preferential removal of inorganic material is evident, whereas organic material removal is not seen. There is approximately 1.2 % loss of minerals. Followed by the *dark zone*, where there is 6% mineral loss per unit volume of enamel. Light passing through this zone causes brown discolouration. The third zone is the *body of the lesion*. There is 24% mineral reduction per unit volume of normal enamel. Next is the *surface zone*. Partial demineralization results in 10% loss of minerals, with broadening of prism sheaths. Forms an intact surface layer with 1 — 5% pore volume. The presence of fluoride, calcium and phosphate in saliva and plaque produces remineralization hence an equilibrium exists which maintains the surface layer but with some overall loss of minerals. The cores of the enamel are rich in carbonate so greater demineralization occurs in the central portion of the crystal when the lesion progress towards the dentino-enamel junction. Affected and infected dentin are separated by a layer of demineralisation. Active lesions are differentiated from the arrested decay by the presence of active bacteria, impermeability to dyes and low calcium content. [25]

Demineralisation in non-carious lesions:

Whenever the teeth surface is covered by acidic or proteolytic corrodent and they are abraded by friction resulting in abrasion/biocorrosion. This can occur when the teeth are brushed with a dentifrice immediately after drinking acidic fluids or after regurgitating or even if the bacterial plaque were present, producing acids and proteases, which acts on the tooth surface, particularly the cervical dentin. *Attrition* is the physiological wearing away of teeth due to bruxism or aggressive cleansing and *abrasion* is the pathological wearing away due to applying excessive force or using a wrong brushing technique. Abrasion usually occurs in the cervical region. *Abfraction* is a pathological lesion seen as angular notches due to bio-mechanical loading. *Erosion* is the progressive loss of hard dental tissue by a chemical process without bacterial action. Lesions occur on the gingival third of the buccal and labial surfaces of tooth usually in labial aspect of maxillary anteriors. The dental hard tissue after extensive erosion show no signs of demineralization except that some enamel is lost due to dissolution of apatite mineral by acids of non-bacterial growth. The mineral content of the remaining enamel is unchanged. Eroded enamel appears hard and shiny. Exposure of demineralized dentin results in faster loss of material with occlusal scooping or cupping of the cusp tips initially and grooving of the incisal edges, enhanced by abrasion from foods. The lesion occurs in elderly suffering from repeated episodes of gastric reflux, leading to periodic cycles of demineralization and remineralization of the exposed root surfaces. [26,27]

Conclusion

The constant consumption of refined carbohydrates has led to an increase in prevalence of dental caries. The dynamic relationship and the delicate balance between demineralization and remineralization plays an important role in the progression or the reversal of the caries process.[28]

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References

1. Ensanya Ali Abou Neel, Anas Aljabo, Adam Strange, Salwa Ibrahim, Melanie Coathup, Anne M Young, Laurent Bozec, Vivek Mudera. Demineralization–remineralization dynamics in teeth and bone. Int J Nanomedicine. 2016; 11:4743–63.
2. Pashley EL, Comer RW, Simpson MD, Horner JA, Pashley DH, Caughman WF. Dentinpermeability: sealing the dentin in crown preparations. Oper Dent. 1992;17(1):13-20.
3. Dawes C. What is the critical pH and why does a tooth dissolve in acid?J Can Dent Assoc. 2003;69(11):722-4.
4. Margolis HC, Zhang YP, Lee CY, Kent RL Jr, Moreno EC. Kinetics of enamel demineralization in vitro. J Dent Res. 1999;78(7):1326-35.
5. Tsai MT, Wang YL, Yeh TW, Lee HC, Chen WJ, Ke JL, Lee YJ. early detection of enamel demineralization by optical coherence tomography. Scientific reports. 2019 20;9(1):1-9.
6. Sabel N, Robertson A, Nietzsche S, Norén JG. Demineralization of enamel in primary second molars related to properties of the enamel. ScientificWorldJournal. 2012;2012:587254
7. Hayashi O, ChibaT, ShimodaS, Momoi Y. Demineralisation, and remineralisation phenomena in acid erosion model. J of hard tissue biology.2016; 25(1): 27-34.
8. Kalra Dheeraj D, Kalra Rinku D, Kini Prajna V, Prabhu CR. Non fluoride remineralisation. An evidence-based review of contemporary technologies. J of Allied Sci. 2014;3(1):24
9. Nabiyouni M, Zhou H, Luchini TJ, Bhaduri SB.Formation of nanostructured fluorapatite via microwave assisted solution combustion synthesis. Mater Sci Eng C Mater Biol Appl. 2014; 37:363-8.
10. Stanic V, Radosavljevic-Mihajlovic AS, Zivkovic-Radovanovic V, NatasijevicB, Marinovic-Cincovic M, Markovic JP, Budmir MD. Synthesis, structural characterisation, and anti-bacterial activity of Ag+ doped fluorapatite nanomaterials prepared by neutralization method. Appl.Surf.Sci.2015;337:72-80
11. Tredwin CJ, Young AM, Abou Neel EA, Georgiou G, Knowles JC. Hydroxyapatite, fluor-hydroxyapatite and fluorapatite produced via the sol-gel method: dissolution behaviour and biological properties after crystallisation.J Mater Sci Mater Med. 2014;25(1):47-53
12. Martins C, Castro GF, Siqueira MF, Xiao Y, Yamaguti PM, Siqueira WL. Effect of dialyzed saliva on human enamel demineralization. Caries Res. 2013;47(1):56-6
13. Mithra N Hegde, Ankit R Sajnani.Salivary Proteins—A Barrier on Enamel Demineralization: An *in vitro* Study. Int J Clin Pediatr Dent. 2017; 10(1): 10–13
14. González-Cabezas C. The chemistry of caries: remineralization and demineralization events with direct clinical relevance. Dent Clin North Am. 2010;54(3):469-78
15. Meurman JH, Rantonen P, Pajukoski H, Sulkava R. Salivary albumin and other constituents and their relation to oral and general health in the elderly. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002;94(4):432-8
16. Kielbassa AM, Oeschger U, Schulte-Monting J, Meyer-Lueckel H. Microradiographic study on the effects of salivary proteins on in vitro demineralization of bovine enamel.J Oral Rehabil.2005;32(2):90-6.
17. Mithra N Hegde, Ankit R Sajnani.Salivary Proteins—A Barrier on Enamel Demineralization: An *in vitro* Study. Int J Clin Pediatr Dent. 2017; 10(1): 10–13
18. Nurelhuda NM, Al-Haroni M, Trovik TA, Bakken V. Caries experience and quantification of Streptococcus mutans and Streptococcus sobrinus in saliva of Sudanese schoolchildren.Caries Res. 2010;44(4):402-7
19. Zhang YP, Kent RL Jr, Margolis HC. Enamel demineralization under driving forces found in dental plaque fluid.Eur J Oral Sci. 2000;108(3):207-13.
20. R. Adhani, Widodo, B. I. Sukmana, and E. Suhartono. Effect pH on Demineralization Dental Erosion. Int J Chem Eng Appl. 2015;6(2):138-141.
21. Razdan TR, Singh VP, Rav AB, Harihara M, Sreeram SR. Comparative Evaluation of Enamel Demineralization Depth by Five Sweeteners: An In. Vitro Study. J Int Oral Health.2016;8(6):709-715.
22. Gwinnett AJ, Matsui A. A study of enamel adhesives. The physical relationship between enamel and adhesive.Arch Oral Biol. 1967;12(12):1615-20.

23. Zafar MS, Ahmed N. The effects of acid etching time on surface mechanical properties of dental hard tissues.Dent Mater J. 2015;34(3):315-209

24. M.K. Pugach, J. Strother, C.L. Darling, D. Fried, S.A. Gansky, S.J. Marshall, G.W. Marshall· Dentin Caries Zones. Mineral, Structure, and Properties. J Dent Res. 2009; 88(1): 71–76.

25. Goldberg M (2020) Enamel and Dentin Carious Lesions. JSM Dent 8(1):1120.

26. Abdulhadi WarrethEyas AbuhijlehMohammad Adel Almaghribi, Ghanim Mahwal,Ali Ashawish. Tooth surface loss. A review of Literature. Saudi Dent J. 2020;32(2):53-60.

27. Yun -Qi-Wu, Joseph A. Arsecularatne, Mark Hoffman. Attrition-corrosion of human dental enamel: A review. Bio surf Bio Tribol.2017. 3(4):196-210

28. Poornima Jose, Malathi Suresh, S. Kavitha, S Mahalakshmi. Mineral loss before and after bleaching and mineral uptake on application of Remineralizing agent. Indian J Multidiscip Dent. 2010. 1(1):47-49.