

## The Biochemical Basis of Dental Caries in Action

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### Abstract

Dental Caries is a complex and multifactorial disease that is based on an environment favouring demineralisation over remineralisation.

Clinicians look to remineralise carious lesions at an early stage to avoid further tooth damage. The fundamentals of our clinical practice are underpinned by the biochemistry of this process, which will be discussed in this review.

**Keywords:** Biochemical; Remineralisation; Demineralisation

### Dental Caries and the Carious Process

Dental caries is essentially a dynamic process involving a microbial deposit, the dental biofilm on the tooth surface, which undergoes several metabolic reactions, resulting in chemical dissolution of the tooth substance [1].

The dental biofilm is a community of metabolically active microorganisms that have adhered to the tooth surface [2]. Bacteria within the biofilm metabolise fermentable carbohydrates from the diet, and organic acids are produced, which dissolve the hydroxyapatite component of teeth [3]. The acidic environment selects for the microorganisms best able to withstand this low pH, therefore these organisms flourish and continue the carious process.

It is the frequency of carbohydrate consumption that plays such a pivotal role in the carious process. Patients who repeatedly ingest high levels of carbohydrates have recurring drops in the salivary pH as the buffering capacity is overwhelmed [4].

The Critical pH is a key biochemical value in the carious process and is 5.5 for enamel, indicating the highest pH at which there is net mineral loss of tissue from the tooth, i.e. the pH at which demineralisation begins.

Dentine is composed of more organic material and water, meaning it is more easily degraded in the carious process and so, the critical pH is higher (more alkaline) at approximately 6.2 [5].

### The Aetiology of Caries

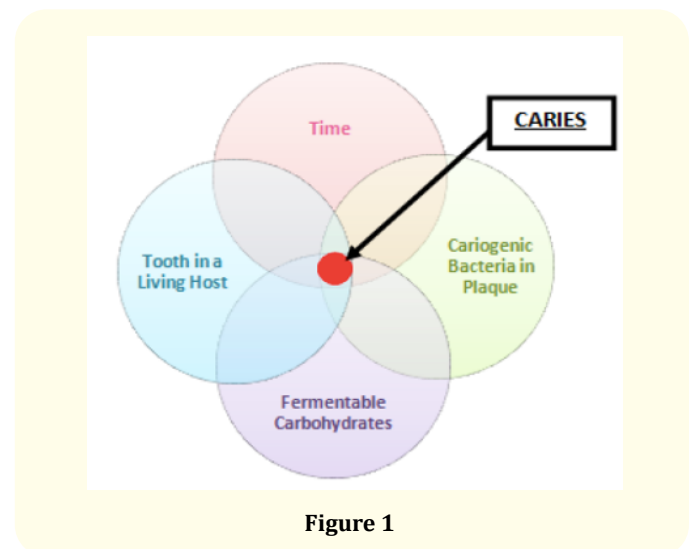


Figure 1

### Biochemistry of plaque

The Dental Plaque Biofilm can be defined as a “three-dimensional structure consisting of densely packed aggregations of microbes” that adhere to the each other and the tooth surface [6]. Attachment of the pioneer species is the earliest phase of biofilm formation. This is subsequently followed by succession of other colonising species, which modify the oral environment to favour the development of a successful climax community [6].

*S. Mutans* is recognised as the principal species in caries due to its property of aciduricity, allowing it to tolerate acidic environments. Thus, during the carious process, *S. Mutans* is able to thrive and multiply as a result of its high tolerance to the low pH environment [7].

*S. Mutans*-derived glucosyltransferases (Gtfs) are important in the process of plaque development. Studies have concluded that specific Gtfs were upregulated in response to a more acidic environment, aiding colonisation by other bacteria and the cohesion of plaque, contributing to a more caries-susceptible environment [8,9].

As plaque matures and the microbiota adapts, there is a change from a *Streptococcus*-dominant to an *Actinomyces*-dominant bacterial community [10].

### Biochemical role of carbohydrates in caries

The concentration of the non-milk extrinsic sugars (NMES) and sucrose, in particular, play the most significant contribution to dental caries [11]. Sucrose is considered to be the dietary carbohydrate that has the highest cariogenic potential with its effects being both frequency and concentration-dependent [12].

The Maillard Reaction involves the biochemical interactions between sugars and proteins that are responsible for the lesion discoloration in the carious process. Otherwise known as the 'Browning Reaction' [13], it is categorised as a non-enzymatic/glycation process [14]. It involves an irreversible change in the amino acid structures that make up proteins, hence altering their function. The reactions that proceed lead to the formation of brown polymers called melanoidins [14], which are responsible for the colour change. The Maillard Reaction has important consequences for clinicians as it has been discovered that the extent of disease can be interpreted from the severity of brown discoloration.

### Biochemistry of demineralisation

Demineralisation begins with increased enamel porosity, which can lead to cavitation and eventually tooth loss if untreated.

Organic acid production (in the form of H<sup>+</sup>) as a result of bacteria digesting sugars causes the pH of plaque to fall, resulting in dissolution of HA into Calcium ions, Hydrogen Phosphate ions and water, which begins the process of demineralisation within enamel [15].

Mineral loss from the enamel which leaches into the surrounding saliva and plaque is ultimately the cause of White Spot Lesion

(WSL) formation [16]. The mineral is replaced by water, which reduces the refractive index and so light cannot enter the enamel rods as far before being scattered back towards the surface [15]. This reflection is responsible for the appearance of the WSL.

Upon remineralisation, a dense layer of Calcium, Phosphate and Fluoride forms on the surface that has greater resistance to further demineralisation [17]. If demineralisation persists, a point is reached where the enamel subsurface has been so reduced that the outer enamel surface cannot support or withstand any biting forces, and so cavitation results [16].

Research has led to the discovery of an innovative type of remineralisation technology with the potential to improve or even completely restore the appearance of a WSL. Casein Phosphopeptides-Amorphous Calcium Phosphate (CPP-ACP) is based upon phosphopeptides from milk casein [18]. Its unique ability to penetrate into the enamel porosities and stabilise Calcium Phosphate allow it to remineralise tooth tissue, eliminating the porous effect and restoring the light properties and translucency to improve the appearance of the WSL [16,18,19].

Demineralisation of dentine results when the critical pH of 6.2 is reached, causing the dissolution of mineral [20]. Two dentine layers form described as an outer (infected) layer and inner (affected) layer. Within the inner carious dentine, the collagen fibrils maintain their shape (and thus can be remineralised) but the collagen within the outer carious dentine (closest to the coronal tooth surface) changes shape due to its degradation [21]. It is the ability to distinguish between the layers during carious dentine removal that is significant in our clinical practice.

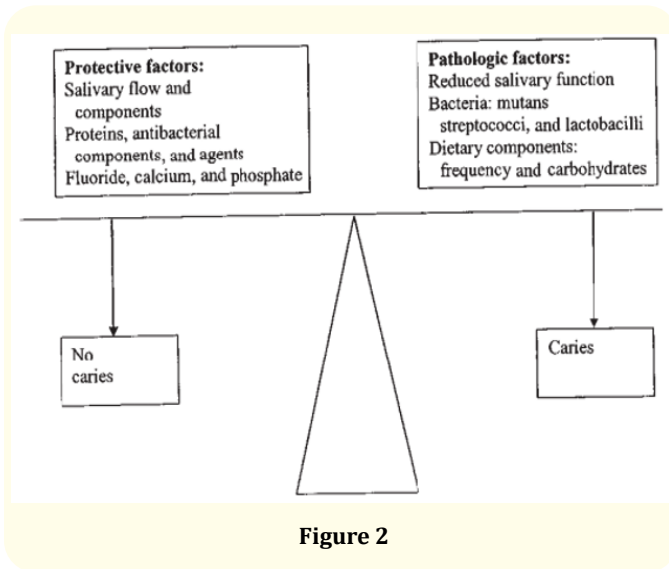
In response to carious attack, the dentine acts to defend itself and the pulp by exhibiting different reactionary mechanisms such as tubular sclerosis – a reaction that remineralises the tubules with "Mg-Substituted  $\beta$ -TCP (Whitlockite)" and apatite crystals [20].

### The carious process

The balance between the pathologic and protective factors (Touger-Decker, van Loveren 2003).

### The biochemistry of saliva in relation to caries

It is the Hydrogen Bicarbonate balance in saliva that is responsible for the buffering capacity and pH, which acts to protect the enamel from caries [22].



Saliva is maintained at neutral pH by the action of buffers including inorganic Phosphate in resting saliva and the Carbonic Acid-Bicarbonate system in stimulated saliva, the latter of which is recognised as the major salivary buffer [22].

An increased salivary flow influences the biochemistry of the carious process as it results in a rise in the concentration of Bicarbonate, Chloride and Sodium [22]. The elevated Bicarbonate concentration neutralises the acids, promoting the remineralisation of tooth tissue [22]. Thus, ensuring our patients have adequate salivary flow is an important contributor to our clinical prevention of caries.

**The enzymes involved in the carious process**

Matrix Metalloproteinases (MMPs) are categorised as Zinc-dependent, host-derived proteolytic enzymes, which are important in the degradation of the organic matrix of dentine in the carious process [5,23].

Research has found that pH changes in the carious lesion activate MMPs [23]. MMPs only function at neutral pH and so the salivary buffer systems neutralise the acidic pH, allowing the MMPs to become activated to degrade the organic matrix of dentine [24].

The activation of MMPs is also dependent on the presence of Zinc. However, interestingly, it has been reported that as well as this, Zinc can influence the signalling pathway of MMPs and result in dentine remineralisation [25]. This makes Zinc an attractive element to exploit clinically as a therapeutic agent for the remineralisation of tooth tissue.

Zinc-leaching dental materials such as amalgams, Zinc Phosphate cement, Calcium Hydroxide and Zinc-Oxide Eugenol cements are thought to inhibit the demineralisation of dentine and promote remineralisation [24,25].

**The carious lesion**

Occlusal, non-cavitated carious lesions with some staining (Fejerskov, Kidd 2013).



**The biochemistry of remineralisation and caries prevention**

Xylitol is now widely recognised as having anticariogenic properties when used as a sweetener. Additionally, cranberries can reduce the glucosyltransferase activity of *S. Mutans*, decreasing bacterial adherence [26]. Furthermore, tea extracts are thought to inhibit salivary amylase activity, reducing the presence of fermentable carbohydrates in the oral cavity [26].

It is well established that the Fluoride anion can inhibit bacterial growth. The anion adheres to the enamel, forming Fluorohydroxyapatite, which is more resistant to acid attack. The antimicrobial property of Fluoride ions involves inhibition of the enzyme *Enolase* in the Embden-Meyerhof-Parnas pathway, and so the bacteria are no longer able to thrive and promote tooth demineralisation in the carious process [27].

**The demineralisation-remineralisation process in oral plaque**

A summary of the influence of the saliva on the demineralisation-remineralisation balance (Stookey 2008).

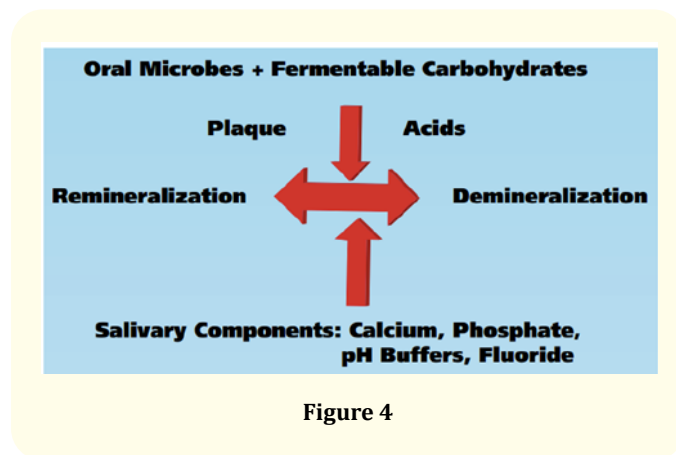


Figure 4

## Conclusion

In conclusion, the scientific knowledge behind caries forms the basis of the decisions made by clinicians on a regular basis, including the extent of caries removal. It also governs the chemical concepts behind anticariogenic agents and other therapeutic means in the treatment and prevention of caries. The knowledge of the biochemistry of dental caries is vital, and always will be, to every clinician and will continuously be applied for generations to come.

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