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To cross link or not

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One of the most important components in dentistry is dentine, which is a complex structure with a high organic component. Majority of its organic component is consisted of collagen type I fibres followed by collagen type III, proteoglycans, MMPs and cysteine cathepsins. Thus, dentine can be introduced as one of the most complex tissues in the human body. The hierarchical arrangement of collagen fibres and the presence of proteoglycans provide dentine the much needed modulus of elasticity to withstand the forces implement on it.

Dentine is one of the two most common substrates in the oral cavity, which dentists encounter in their daily routine treatment procedures. Dentine exposure can happen through caries, mechanical or even chemical trauma and presence of abundant collagen matrix and various bioactive molecules makes it a challenging tissue to work with. Dentine bonding is a unique bond as it binds a non-biological material to biological dentine. The bond created needs to be able to provide support to the remaining tooth structure in order to withstand various stresses within the oral cavity. However, the hydrophilic nature of collagen matrix and activation of collagen degrading enzymes in demineralized dentine matrix affect the durability of these bonds.

Recently, collagen cross-linkers have been introduced in dentistry with various beneficial effects on bonding to dentine as well as on remineralisation of dental hard tissues. Both, natural and artificial collagen cross-linkers such as glutaraldehyde, genipin, grape seed extract and carbodiimide have been tested on their effects on collagen matrix. Collagen cross-linkers can induce bondage among fibrils and increase the intrinsic modulus of elasticity [1]. This enhances both elasticity and strength of the fibre matrix through intermolecular cross-linking. Furthermore, they can inhibit the collagen degrading enzymes [2]. Apart from enhancing the mechanical properties of the dentine matrix, they can also increase bond strengths when used as a pre-treatment agent in both etch and rinse as well as self-etch adhesives[3]. Additionally, certain collagen cross-linkers can promote remineralization of artificial dentinal lesions when combined with a remineralizing agent.

Prior to be used in clinical practice, collagen cross-linkers need further testing and clinical trials. However, its potential use in clinical dentistry must be apprehended. Certain in vitro studies have introduced collagen cross-linkers as pre-treatment agents to be used as an important addition in etch and rinse adhesives [3]. Furthermore, as another study proposed, it would definitely be worthy to incorporate collagen cross-linkers in to etching agents as it will not add any extra steps in the bonding procedure. The most feasible method will be to incorporate in to an adhesive, which is yet to be improved and modified to maintain the quality of the adhesive [4]. In the context of remineralization, it was proposed to incorporate cross-linkers to already available remineralization agents. Therefore, collagen cross-linkers can promote mineral dissolution as well as harden the collagen matrix and resist further break down by collagenase. Moreover, when collagen fibres were treated with certain cross-linkers, they obtain the ability to attract calcium and phosphate molecules and initiate mineral deposition. Thus, further studies are necessary to identify their effects on biomineralization of collagen fibres.

Simultaneously, clinical applications of cross-linkers need further analysis on their cytotoxicity and biocompatibility with the oral mucosa. Furthermore, it is necessary to implement strategies to maintain long term effects of the cross-linkers and to evaluate their effects. Recent studies have thoroughly discussed the reversible protease inhibitory action of the cross-linkers and have found although this action is reduced with time, certain cross-linkers at higher concentration can maintain it for a longer time [5]. During dentine bonding, collagen cross-linkers reduce or inhibit initial nano-leakage through the interface of the resin-dentine bond compared to that of control groups, however, after 18 months, nano-leakage gradually increases[4]. It would be beneficial to find ways to maintain continuous supply of collagen cross-linkers in to the hybrid layer to maintain its stability over time using sophisticated drug delivery methods.

Collagen cross-linkers have been tested on wide array of applications in dentistry. However, they still have the potential to be used in various additional clinical procedures. Many collagen cross-linkers have strong affinity towards proteins. They can stabilize protein molecules and therefore, can be used for fixing the tissue samples. Thus, the natural collagen cross-linkers may safely be used as pulp capping or mummification material during pulp exposures. Besides, their biological actions can be used to maintain tissue integrity in treating periodontitis. Anti-bacterial activity of certain collagen cross-linkers can be utilized to inhibit cariogenic bacteria in the oral cavity. With all these currently tested and prospective applications, collagen cross-linkers would be a timely addition in dentistry.

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