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# Enamel Matrix Derivatives (EMD) in Periodontics - Biomimicry Revisited

Krishnaprasad Kondajji Ramachandra [1,*], Radhika Kumar [2], Saravanan Sampoornam Pape Redy [1] and Delfin Lovelina Francis [3]

[1] *Department of Periodontology, Army Dental Centre (Research & Referral), New Delhi, Delhi, India.*
[2] *ECHS Polyclinic, Gurgaon, Haryana, India.*
[3] *Saveetha Dental College & Hospital, Chennai, Tamilnadu, India.*

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## Abstract

Enamel matrix derivatives are a class of xenogeneic proteins that have shown considerable clinical and histological improvements in periodontal wound healing. The proteins array is currently undetermined in its entirety, however it has been extensively studied in periodontal regeneration. It has resulted in true periodontal regeneration, with the formation of all periodontal structures resembling the developmental stages of periodontal structures. The biological cues in this chemical have received FDA approval for human usage in periodontal practise. It is employed in a variety of surgical treatments, including root covering surgery, periodontal regenerative surgery, bone regeneration, ridge augmentation techniques, and has gained popularity in difficult implant regenerative procedures. The creation of this sophisticated biomolecule-based protein concentration is a godsend to periodontists.

**Keywords:** Enamel Matrix Derivatives; Regeneration; Amelogenins; Periodontics

## 1 Introduction

One of the recent introductions to regenerative periodontics is the use of Enamel Matrix Derivatives (EMD). EMD is a group of enamel matrix proteins derived from enamel organ of porcine origin. The major constituents of Enamel Matrix Derivatives are amelogenins, which are hydrophobic proteins derived from a single gene by alternative splicing and post secretory processing [1].

EMD refers specifically to a purified extract of the naturally occurring enamel matrix proteins, found in large amounts during the secretory stage of crown development. The proteins of the enamel matrix can be divided into 2 major groups

- Amelogenins
- Enamelins.

Amelogenins make up 90% of EMD, with the remaining 10% containing non amelogenins like Proline rich enamelin, sheathilin, amelin, tuftelin, tuft protein, serum proteins and salivary proteins. Nonamelogenins bind to hydroxyapatite (HA) on the tooth surface, and would require a chelating agent such as EDTA to extract them from the mineral

Deposition of enamel matrix proteins on the root surface sets in motion, a series of events that lead to generation of the periodontal attachment apparatus. This phenomenon consists of connective tissue fibers (later called Sharpey's fibers)

* Corresponding author: Krishnaprasad Komdajji Ramachandra
Department of Periodontology, Army Dental Centre (Research & Referral), New Delhi, Delhi, India.

getting trapped along with alveolar bone and cementum. This process takes months to completely surround the developing tooth [2].

Periodontal regeneration mediated by EMD is based on a different concept. It is believed that EMD, when used in periodontal lesions, mimics the development of the tooth supporting apparatus during tooth formation. This phenomenon is termed 'Biomimicry'. Research in the field of use of enamel matrix derivatives was pioneered by Hammarstrom who extensively studied EMDs in animal models. The only commercially available product using EMD is called Emdogain. EMD, which is the active component of Emdogain, is largely insoluble at physiological pH and temperature. The commercial formulation of Emdogain is prepared in a vehicle of propylene glycol alginate (PGA) gel at an acidic pH which allows application of the gel via a syringe to the affected site. Originally the product consisted of EMD and a vehicle solution (Propylene Glycol Alginate) that had to be mixed before use. In order to save time and simplify the procedures a ready-to-use Emdogain gel was developed.

*In vitro* studies have demonstrated that EMD affects cellular attachment, mitogenesis, biosynthesis and differentiation. Enamel matrix derivative coated surfaces improved attachment of periodontal fibroblasts but had no effect on gingival fibroblasts and epithelial cells indicating a selective behavior considered advantageous in the early stages of healing [3].

Enamel matrix derivatives increase the attachment rate, growth rate and the metabolism of cultured periodontal ligament cells. Studies have shown that EMD favors the growth of mesenchymal cells as compared to epithelial cells. Periodontal cells exposed to EMD secrete autocrine growth factors which contribute to periodontal tissue healing and regeneration mimicking natural tooth development. As it is known that extracellular matrices have the capacity to bind and retain polypeptides, Gestrelius et al. set out to determine whether specific growth factors or adhesion molecules maybe associated with EMD. Gestrelius etal concluded that EMD do not contain any kind of growth factors, but it has been reported by many researchers that EMD has TGF like and BMP like activity. Exact nature of these activities still remains debatable.

Wennstrom J L and Lindhe J studied the effects of enamel matrix proteins on wound healing in the dento–gingival region. They reported a low degree of post treatment discomfort with the use of EMD. They concluded that EMD enhances the early healing of periodontal soft tissue wounds [4]. There are reports of better early healing and less patient discomfort following open flap debridement with adjunctive use of EMD compared to open flap debridement alone. Enhanced synthesis of growth factors and ability of EMD to modulate bacteria could be the reason for increased rate of wound healing seen in case of EMD.

Heijil etal in 1997 demonstrated histological evidence of periodontal regeneration following the use of EMD in humans. Histological examination revealed the formation of acellular extrinsic cementum, which was firmly attached to the underlying dentin surface. The new cementum was thin with inserting collagen fibers which extended into periodontal ligament. Newly formed alveolar bone attached to the periodontal ligament was also present. This case report was first to demonstrate that EMD had the potential to promote true regeneration of a functional periodontal attachment [5]. Cochran et al have evaluated the histological regeneration of the periodontal tissues in the baboon following the application of EMD. In these experiments, periodontal defects ranging from 1 to 6 mm were created bilaterally around three teeth in the mandible. Plaque was allowed to accumulate around ligatures were placed in the defects. All defects were debrided and treated with EMD. After 5 months the teeth associated were histologically evaluated. The results demonstrated that periodontal regeneration occurred in all sizes of defects. In many cases dramatic formation of cementum, periodontal ligament and bone was reported far coronal to the notch at the base of the defects [6].Another study using the same model used EMD in combination with an autogenous bone graft in the periodontal defects. Significant amounts of periodontal regeneration occurred in lesions treated with EMD and bone graft than in control lesions, again dramatic amounts of new cementum; periodontal ligament and bone were formed far coronal to the base of the defect [7]. In an experimental animal study the use of EMD was evaluated in experimentally created dehiscence and recession type defects. Histological assessments demonstrated 80 to 90% regeneration of periodontal tissues. Rasperini and coworkers in the year 2000 used EMD as an adjunct to sub epithelial connective tissue grafts in a patient and found histological evidence of periodontal regeneration [8]. More recently McGuire and Cochran demonstrated histological evidence in humans of new cementum formation with organizing periodontal ligament fibers and islands of condensing bone following the use of a coronally advanced flap with adjunctive use of EMD [9]. Hagewald et al in 2002 followed 36 cases where EMD was used as an adjunct to coronally advanced flap for 12 months post operatively. This was a split mouth study and he reported that there is no additional benefit of EMD in the overall clinical outcome [10]. In the same year Ignazio Berlucchi et al used EMD on 26 recession cases in 14 patients and concluded that use of EMD displays good clinical results, which is comparable to or superior to other techniques [11].

## 2 Conclusion

Convincing results outlining a reduction in probing pocket depth (PPD) and formation of new cementum and bone have been reported in clinical trials, metaanalysis studies, and Cochrane systematic review. Despite the clinical success of EMD, the specific mechanisms by which periodontal regeneration occurs following its application, remains a matter of scientific debate. Further studies in this regard would help to understand these mechanisms and clinical applications of EMDs.

## Compliance with ethical standards

*Disclosure of conflict of interest*

The authors declare no conflicts of interest.

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