IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 8 Ver. IV (Aug. 2015), PP 30-35
www.iosrjournals.org

Bioactive Glass Nanoparticles (NovaMin®) for Applications in Dentistry –

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***Abstract*:** *Calcium Sodium Phosphosilicate (NovaMin®) have been used in bone and tissue regeneration for over 15 years. It is effective as an adjunct to conventional surgery in treatment of intrabony defects. It has also been incorporated in dentifrices as a remineralising ingredient for treating dentinal hypersensitivity. Recent studies with NovaMin containing dentifrices and the particulates mixed with water alone have been shown to possess a strong anti-microbial action against periodontal pathogens that could be of significant benefit to the patient in periodontal maintenance therapy. The dentifrice containing Bioactive glass significantly improves gingival health as measured by a reduction in gingival bleeding and reduction in supragingival plaque. Thus, in the present review, an attempt is made to discuss the various benefits of NovaMin in periodontal therapy.*
Keywords: *NovaMin, dentinal hypersensitivity, anti-microbial, bioactive glass, periodontal therapy.*

I. Introduction

NovaMin® is the branded ingredient that is found in a number of professional use and over-the-counter dental products designed to give immediate and long-lasting relief from tooth sensitivity. NovaMin® and the other (Calcium Sodium Phosphosilicate) CSPS materials were originally developed as bone regenerative materials. In the early 1970's, CSPS materials are part of the broader class of bioactive ceramics which included calcium phosphate materials and calcium hydroxyapatite materials that have been developed for hard tissue repair and replacement, by Professor Larry Hench at the University of Florida, mainly due to their chemical similarity to bone mineral. [1] It is instructive to understand the science behind the unique properties and reactivity of the CSPS materials, and how the science that was developed for bone regenerative medicine translated directly to the area of oral health care. Fig 1 shows the bonding interface of CSPS, 45S5 bioactive glass taken from a 3-month implant in a rat tibia.

Recently, anti-microbial properties inherent in NovaMin® have been described. [2-4] One of these compositions has recently been formulated into a dentifrice and has demonstrated strong anti-microbial behaviour in vitro as well as in vivo. While the exact mechanisms of the anti-microbial activity have not yet been fully established, it is likely that the high rate of ionic release and local changes in oral pH seem to play a major role. [5, 6]

This article briefly reviews the various advantages of NovaMin® in the field of dentistry. Specifically, periodontics is the largest field to take advantages of this material. NovaMin® proved to be effective, in reducing dentinal hypersensitivity, as a bone and tissue regenerative material and as an antiplaque and antigingivitis agent. In preparing this review, all English language articles published between 1971 (the first report of bioactive glass) and 2015 were accessed electronically using automated searches. The PubMed database and Google search engine were searched with keywords, including: bioactive glass, clinical application of Novamin and bioactive glasses in dentistry. We reviewed the abstracts of over 150 articles and short-listed 55 articles and scientific proceedings on the basis of their relevance to the review topic. Articles reporting similar findings were excluded. The final articles were printed and studied in detail.

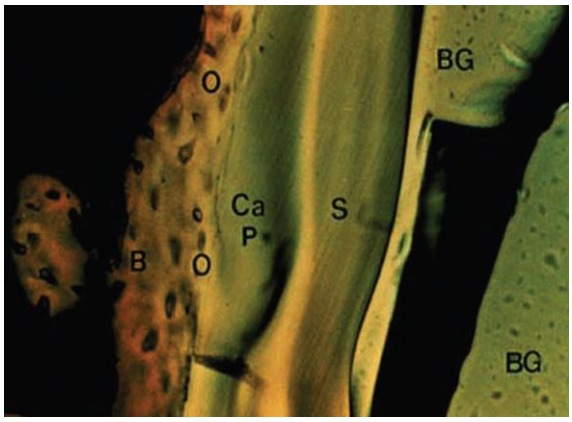

Figure 1. This figure shows the bonding interface of CSPS, 45S5 bioactive glass taken from a 3-month implant in a rat tibia. BG= bioactive glass, S = silica rich layer, CaP = calcium phosphate layer, O = osteoblasts, B = new bone formation.

(Courtesy of Prof. Larry Hench)

II. Composition Of Novamin

NovaMin® is the brand name of a particulate bioactive glass. NovaMin® is technically described as an inorganic amorphous calcium sodium phosphosilicate (CSPS) material that was designed based on a class of materials known as bioactive glasses. It comprises 45% SiO2, 24.5% Na2O, 24.5% CaO and 6% P2O5.[7] The particular composition of NovaMin® is identical to that of the best known bioactive glass material, Bioglass®, and contains only calcium, sodium, phosphate and silica, all as an amorphous matrix. Its chemical formula is CaNaO6PSi. NovaMin® delivers silica and ionic calcium, phosphorus and sodium, which are necessary for bone and tooth mineralization. It was developed and patented by NovaMin Technology, Inc. [8]

III. Uses Of Novamin

At present, bioactive glasses have a wide range of clinical applications in both medicine and dentistry.[9] The first reported clinical application of bioactive glass was the treatment of conductive hearing loss for the reconstruction of the bony ossicular chain of the middle ear.[10] It has been proposed as the material of choice for bone regeneration, [11] hypersensitivity, [12] antigingivitis and antiplaque effect.[13] It is also used for implant coating, as air-abrasive particles to remove carious enamel and dentine, [14] as a dental material to improve the bonding of the restorative material to dentin,[15] as a root conditioner, [16] stain removing agent [17] and in endodontic treatments. [18]

IV. Bone And Tissue Regeneration

NovaMin® has the property to promote adsorption and concentration of proteins utilised by osteoblasts to form a mineralised extracellular matrix and thus promote osteogenesis by allowing rapid formation of bone. It also may act as a barrier retarding epithelial down growth and demonstrates antimicrobial property in vivo. [3] According to the clinical, histological, and radioactive analysis of Schepers, [19] a particle of bioglass forms a protective vesica and grows an independent columella in its centre, irrespective of surrounding bone, which is facilitated by its narrow size and subsequently functions as a pivot for recovery. Lovelace [20] compared the use of bioglass to demineralised freeze dried bone allograft in the treatment of human periodontal osseous defects and concluded that bioglass is capable of producing results in the short-term (six months) similar to that of Decalcified Freezed Dried Bone Allograft when used in moderate to deep periodontal osseous defects. Various workers have demonstrated improvements in clinical parameters like reduction in probing depths, gain in clinical attachment, improvement in osseous fill with bioglass. Due to the merits of bioglass, it is one of the preferred alloplast.[21,22]

V. Application As A Coating Material For Dental Implants

Although hydroxyapatite can be sprayed on the surface of dental implants as a bioactive coating material, its use has unavoidable drawbacks. [23] Implant coatings require good adherence to metal substrate. Titanium implant surfaces are routinely coated with hydroxyapatite to produce this rough surface and improve osseointegration, but their adherence to the metal is not ideal. [24] Consequently, researchers have studied components to improve physical compatibility with titanium.[25] BioglassTM may be used as an alternate osteoproductive, abrasive surface material for implants. [26] However, more research is needed for bioactive glasses to be used clinically as a coating material for dental implants.

VI. Antihypersensitivity Effect

A number of theories have been proposed over the years to explain the pain mechanism of dentinal hypersensitivity. An early hypothesis was the dentinal receptor mechanism theory which suggests that dentine hypersensitivity is caused by the direct stimulation of sensory nerve endings in dentine. [27] Also, odontoblast transducer mechanism theory proposed by Rapp et al., [28] suggested that odontoblasts act as receptor cells, mediating changes in the membrane potential of the odontoblasts via synaptic junctions with nerves. The currently accepted hypothesis is the hydrodynamic theory which states that dentine hypersensitivity may be caused by movement of the dentinal tubule contents. [29]

Several products have been used to manage dentinal hypersensitivity, which either prevent the conduction of pain impulses or mechanically occlude the dentinal tubules, but present highly variable results. [30-34] The best way to remineralize enamel is the most natural way, through the saliva. NovaMin® (calcium sodium phosphosilicate) is a new material available, which when exposed to water/body fluids (saliva), reacts instantly by releasing billions of mineral ions that become available to the natural remineralization process in the mouth. It deposits hydroxycarbonate apatite and reduces the possibility of reopening the dentinal tubules. Fig 2a shows prepared dentin slab showing open tubules. Fig 2b showing dentin after one application of NovaMin for two minutes and a 30-second water rinse. NovaMin is made from the same bioactive material, which is used in the most advanced bone regeneration material. And as it is made with the same minerals naturally found in saliva, it is safe and non-toxic. [1,35] Table 1 list down some currently available NovaMin-containing products.

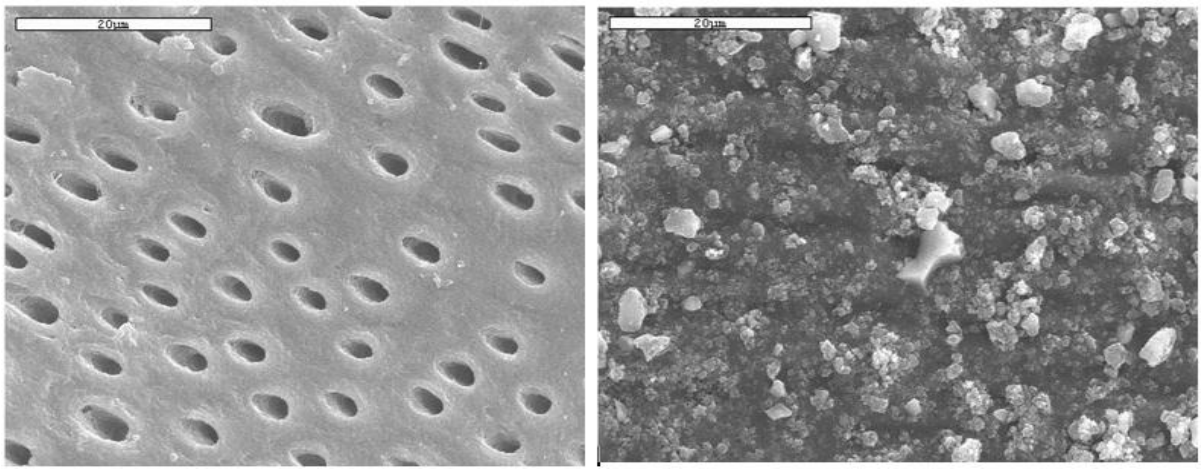

Figure 2. a. Prepared dentin slab showing open tubules. b. Dentin after one application of NovaMin for two minutes and a 30-second water rinse. (Courtesy:- David C. Greenspan. NovaMin and Tooth sensitivity- An Overview. J Clin Dent 2010;21:61-5.)

Table 1: A list of some currently available NovaMin- containing products

PRODUCT	DESCRIPTION
Vantaj (India)	5.0% NovaMin
SHY-NM (India)	5.0% NovaMin
Sensodyne Repair and Protect (EU,UK, Canada, India and Brazil)	5.0% NovaMin
SootheRx (US)	7.5% NovaMin, daily use, professionally supplied
X-Pur (Canada)	5.0% NovaMin, daily use
Nanosensitive (Germany)	7.5% NovaMin
Sensishield (UK)	5.0% NovaMin
Nutri-émail (France)	7.5% NovaMin
Odontis Sensiblock (Brazil)	7.5% NovaMin

VI.I In Office Novamin Application

In-office chair side desensitization using NovaMin® powder over the exposed dentinal tubules, provide an advantage over home use of desensitizing agents as they do not require multiple applications, patient compliance is not required and higher concentration of the desensitizing agent can be used that provides better relief from sensitivity. This in-office procedure proved to be a therapeutic adjunct to provide rapid precipitation and blocking of tubules and filling in of surface defects with NovaMin®, and providing immediate relief for the patient with hypersensitive teeth. **[36]**

VII. Antiplaque And Antigingivitis Effect

Recently, anti-microbial properties inherent in these materials have been described. One of these compositions has recently been formulated into a dentifrice and has demonstrated strong anti-microbial behavior in-vitro as well as in-vivo. Stoor et al. **[2]** first published results of exposure of planktonic organisms known to be involved in the progression of gingivitis and periodontitis to particulate bioactive glass compositions. In these studies, it was found that exposure of a 40% solution of bioactive glass to the cultures for 10 min resulted in a 3 log reduction in Actinobacillus actinomycetemcomitans and total loss of viability of the organism with a 60 min exposure. Similar results were found in Porphyromonas gingivalis. Actinomyces naeslundii lost total viability in a10 min exposure to the bioactive glass as did Streptococus mutans. Allan et al, **[3]** using particulates of bioactive glass with a size range from 300 to 500 mm, showed an antibacterial effect against S. mutans, S. sanguis, P. gingivalis, Furobacterium nucleatum, A.actinomycetemcomitans and Prevotella intermedia with a 1-h exposure to the particulates. The percentage kill ranged from 51% against S. mutans to 100% kill of P. intermedia.

Allan et al **[3]** also studied this composition against mixed species biofilms derived from human saliva and found that the viability of the biofilms exposed to the bioactive glass was significantly reduced compared with biofilms exposed to a bio-inert glass. One of the authors recently showed that fine particulate bioactive glass (NovaMin®) incorporated into a non-aqueous dentifrice was able to reduce the viability of planktonic bacterial cultures of S. mutans, F. nucleatum, A. Naeslundii and S. sanguis. A 2-min exposure to a 1:3 dilution of both 3% and 10% bioactive glass-containing dentifrice reduced the viability of these organisms by 4.5 log against F. nucleatum to total loss of viability of the S. sanguis culture.

A study carried out by Eberhard et al **[37]** showed that the topical application of 45S5 bioactive glass in humans with experimental gingivitis attenuated the clinical signs of inflammation. Rectenwald JE et al **[38]** observed that peritoneal cavity of a mice produced instant anti-inflammatory response by early induction of IL-6 when exposed to Bioglass® and thus support the fact that it could be used as an anti-gingivitis ingredient. Tai BJ et al **[13]** which demonstrated that a dentifrice containing Novamin® significantly improves oral health as measured by a reduction in gingival bleeding and reduction in supragingival plaque compared with a negative dentifrice over the 6 weeks study period.

VIII. Mechanism Of Action

In bone regeneration, bioglass particles not only show osteoconductivity, but also an osteostimulatory effect. The pore size of bioglass allows an optimal space for vascularisation. It is also easy to manipulate and has a haemostatic effect.**[1]** In the treatment for dentinal hypersensitivity the physical occlusion of Novamin® particles begins when the material is subjected to an aqueous environment. Sodium ions (Na^+) in the particles immediately begin to exchange with hydrogen cations (H^+ or H_3O^+). This rapid release of ions allows calcium (Ca^+) ions in the particle structure, as well as phosphate (PO_4^{3-}) ions to be released from the material. This initial series of reactions occurs within the seconds of exposure, and the release of the calcium and phosphate ions continues so long as the particles are exposed to an aqueous environment.**[1]** A localized, transient increase in pH occurs during an initial exposure of the material due to the release of sodium. This increase in pH helps to precipitate the calcium and phosphate ions from the Novamin® particle, along with the calcium and phosphorus found in saliva, to form a calcium phosphate (Ca-P) layer. As the particle reactions continue and the deposition of Ca and P complexes continue, this layer crystallizes into hydroxycarbonate apatite, which is chemically and structurally equivalent to biological apatite. The combination of the residual Novamin® particles and the hydroxycarbonate apatite layer results in the physical occlusion of dentinal tubules, which will relieve the hypersensitivity.**[39]** Allan ascribed much of the effect of the bacterial kill to an increase in pH of the bioactive glass in solution, although it appears that the release of large quantities of calcium from the bioactive glass might also play a role in the observed behaviour towards the microbes.**[3]**

IX. Other Advantages Of Novamin

A very recent in vitro study evaluated the effect of Novamin® desensitising toothpaste mixed with 15% carbamide peroxide on tooth bleaching and tubule occlusion. It was found that the addition of Novamin® to 15% Carbamide peroxide occluded the dentinal tubules and that it did not affect the bleaching procedure. They also emphasized its clinical relevance in a dual advantage of desensitizing and bleaching with a single paste system.**[40]** Recent studies have also demonstrated a potential for Novamin® to prevent demineralization and/or aid in remineralization of white-spot lesions. NUPRO® NUSolution TM with NovaMin® is the newest Dentsply Professional prophy paste. It is currently the only product powered by NovaMin, delivering the triple benefit of tooth desensitization, tubule occlusion and stain removal.**[41]**

X. Drawbacks Of Novamin

Apatite formation and blocking of the dentine tubules may however take several weeks with NovaMin. Patients are looking for an immediate relief of dentin hypersensitivity and pain. A tooth paste that acts more quickly to block the dentine tubules is likely therefore to provide more noticeable benefits to the individual, and this may equate to a greater uptake in toothpaste formulations for dentine hypersensitivity. The 45S5 glass has a hardness of about 4.7 GPa compared to enamel at about 3.5 GPa. In terms of abrasive wear during tooth brushing, it would be desirable to have a glass that is similar to the hardness values of natural enamel in order to minimize the loss of enamel. **[42]**

XI. Conclusion

The wealth of science behind the development of this class of materials has led to investigations of NovaMin for oral healthcare applications beyond the treatment of tooth sensitivity. The potential of these materials for remineralization of both enamel and dentin has been studied in vitro and in situ and holds promise. In addition, the unique ionic reactions and potential antimicrobial and anti-inflammatory properties might prove useful in treating gingivitis. However, it should be noted that most of the supporting data have been overwhelming from in vitro studies. Further longitudinal studies are necessary as at present, insufficient well-designed and controlled clinical studies exist that allow systematic and meta-analysis review of NovaMin in all of its suggested clinical indications.

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