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Review on Theobromine: An Alternative to Fluorides in Treating Dentinal Hypersensitivity

Shailee Chandak[1], Priyanka Paul Madhu[1*], Kumar Gaurav Chhabra[1], Amit Reche[1], Gopika Mahure[1], Shefali Giri[1] and Manoj Chandak[2]

[1]Department of Public Health Dentistry, Sharad Pawar Dental College and Hospital, DMIMS (Deemed to be University), Sawangi (Meghe), Wardha-442001, Maharashtra, India.
[2]Department of Conservative and Endodontic, Sharad Pawar Dental College and Hospital, DMIMS (Deemed to be University), Sawangi (Meghe), Wardha-442001, Maharashtra, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Theobromine is a unique constituent that can help dentistry and general health in the future. The generic name of theobroma is obtained from two Greek words i.e., Theo and Broma, which means "food of the gods". It can be found in cocoa beans and chocolates. Theodent toothpaste harness the power of cocoa. Rennou, the main component in Theodent, is a unique compound that combines theobromine, calcium, and phosphate to enhance enamel remineralization. This article is to review the effectiveness of theobromine in blocking dentinal tubules by preventing dentinal hypersensitivity, and its positive effects on general health. Various researches and valid documents were reviewed by us. Several studies have been conducted that shows theobromine is effective in blocking dentinal tubules, thus preventing dentinal hypersensitivity as well as tooth demineralization. It also has other general health benefits. Because of its potent vasodilation, diuretic and heart stimulant effect, theobromine can also be used in treating high blood pressure. It also aids in opening of airways and helps in preventing kidney stones. The use of fluoride dentifrices is debatable, as it has many detrimental effects. Also, we consider that theobromine if used as a component in dentifrices, if unintentionally swallowed, cause no catastrophic effects.

**Corresponding author: E-mail: drpriyanka0690@gmail.com;*

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1. INTRODUCTION

Dentinal hypersensitivity is a major difficulty seen in day to day clinical practices. It can be marked as pain emerging from the dentin which gets exposed as result of thermal, osmotic, chemical or tactile stimuli and is not associated with any other type of dental defect or disease [1].

According to the most widely recognised hypothesis for dentinal hypersensitivity, chemical or physical changes disrupt the fluids of the exposed canaliculi. Movement of intratubular fluid excite baroreceptors in the pulp and inside the dentin, which causes neural discharge and a painful feeling [2].

For the dentinal hypersensitivity to occur, dentin must be exposed. Dentine can be exposed in a variety of ways. It may be due to denudation of dentin surface which is usually covered by cementum or enamel as result of attrition, abrasion or erosion. Also, in certain cases, enamel or cementum that usually covers the dentine does not meet, exposing the dentin and causing a developmental abnormality [3,4].

Generally, it is seen that dentinal hypersensitivity is rarely caused by single factors, but as combination of several. Whatever be the cause of dentine exposure, one characteristic appears to be usual: exposed dentinal tubules, which serve as a direct passage between internal pulp and external surface of tooth. It is not possible if the tubules are not exposed [5].

Dentinal hypersensitivity is still an underappreciated issue in day to day practices, as most of the patients develop contriving strategies.

The current techniques in treating dentinal hypersensitivity uses chemical agents, that represses and/or alter the coded signal that travels along nerve cell membrane by occluding the dentinal tubules to decrease dentinal permeability and prevent fluid flow, which in turn reduces discomfort/pain. Fluorides are commonly used as chemotherapeutic agent for dentinal hypersensitivity as it is quite inexpensive and can be administered through variety of cost effective methods. But, Antifluoride lobby is mounting pressure because of the rising side effects of fluorides. Alternative agents would clearly be beneficial in treating hypersensitivity [6].

Potassium nitrate can be used either as a mouthwash or a toothpaste. Commercially available toothpaste containing potassium nitrate are Sensodyne ProEnamel®, Crest Sensi-Relief plus Scope Toothpaste, Colgate®, Sensitive Pro-Relief. Though, its effectiveness is doubtful, but it is evident that K^+ ions found in paste or gel dentifrice that contain 5% KNO_3 can minimize the irritability of A fibres encircling the odontoblasts which helps in relieving sensitivity effectively [7,8]. It is the most recent therapeutic approach of dentin tubule occlusion.

Precipitative intratubular occlusion was attained by some pastes or aqueous solutions which contain ferric oxalate, potassium oxalate and glutaraldehyde [9]. However, current evidence does not support the recommendation of oxalate treatment for dentin hypersensitivity [10]. Hazards related to glutaraldehyde cannot also be neglected [11]. Lately, superior clinical outcomes are obtained with products which contains calcium sodium phosphosilicate (NovaMin®), calcium carbonate, or strontium acetate [12, 13].

The first FDA-approved agent, Fluoride varnish is also used for the treatment of hypersensitivity by forming a calcium fluoride protective layer. But high levels of fluoride can cause certain side effects such as mental retardation, Down's syndrome, thyroid problems [14,15]. Adhesive bonding techniques which are used to seal the tubules were also used, but because these bonding agents lack fillers, they tend to wear easily [16].

1.1 Theobromine

'Xantheose' is another name for Theobromine. It is a bitter, crystalline alkaloid of the cacao plant, with the chemical formula C7H8N4O2 [17]. The generic name of theobroma is obtained from two Greek words Theo and Broma, which means 'food of the gods' [18]. Chocolate and a number of other foods, such as tea leaves, may contain theobromine. Its levels in dark chocolate are greater than in milk chocolate [19]. It is similar to the compounds theophylline and caffeine. In spite of its name, the compound does not contain bromine.

Theobromine, an odourless white coloured luminous powder has a resentful taste and a pH of saturated solution as 5.5 to 7.

Theobromine, a structurally related component, is found in high amounts in cocoa. Cocoa was thought to be a good nutrient and even a medicine. Traditionally, the high antioxidant content of Theobroma cocoa beans has been linked to the health benefits of cocoa. The direct psychoactive effect of methylxanthines in cocoa, on the other hand, is remarkable. Caffeine and theobromine are present in parts in cacao. Theobromine which is present in higher concentrations than caffeine is responsible for multiple effects ascribed to cocoa consumption. Theobromine works by inhibiting phosphodiesterases and blocking adenosine receptors [20].

Theodent 300 is the commercially available product that contains theobromine. Theodent toothpaste harness the power of cocoa. Rennou, the main component in Theodent, is a unique compound that combines theobromine, calcium, and phosphate. It is a fluoride free toothpaste and is effective at remineralizing tooth enamel and reducing hypersensitivity.

1.2 Action of Theobromine on Human Body

Theobromine is a vasodilator, diuretic, and stimulant of the heart. Theobromine causes an increase in urine. It helps in preventing kidney stones by increasing urine flow. The diuretic effect and ability to dilate blood vessels enables theobromine in treating high blood pressure. According to the American Journal of Clinical Nutrition, theobromine has a long history of use as a treatment for other circulatory issues such as atherosclerosis and certain vasculitis [21]. Theobromine aids in opening of the airways, which may improve lung capacity and aid in treatment of various respiratory disorders. This effect may be due to theobromine's anti-inflammatory properties. It has ability to lower the levels of inflammatory cytokines including IFN-y and TNF-a. Theobromine raises the levels of HDL (good) cholesterol and reduces LDL (bad) cholesterol.

When consumed in proper doses, theobromine appears to be safe. Long-term daily doses of up to 1,500 mg can have negative consequences such as nausea, loss of appetite, headaches etc. [22].

1.3 Action of Theobromine on Tooth

An invitro study was undertaken by Premnath P, John J, Manchery N, Subbiah GK, Nagappan N, Subramani P et al. on Effectiveness of Theobromine on Enamel Remineralization. It has been demonstrated that theobromine in an apatite-forming medium, strengthens medium's remineralisation ability. It has ability to remineralise the demineralised tissue of the tooth. After treating enamel lesions that has been created artificially with theobromine, it was discovered that theobromine increased the micro hardness of the enamel. Saliva that has been synthesised had no effect on enamel remineralisation. Theobromine increased mineral gain faster than fluoride. Theobromine makes teeth at less risk to bacterial acid erosion by increasing apatite crystals size which form and reinforce enamel [23].

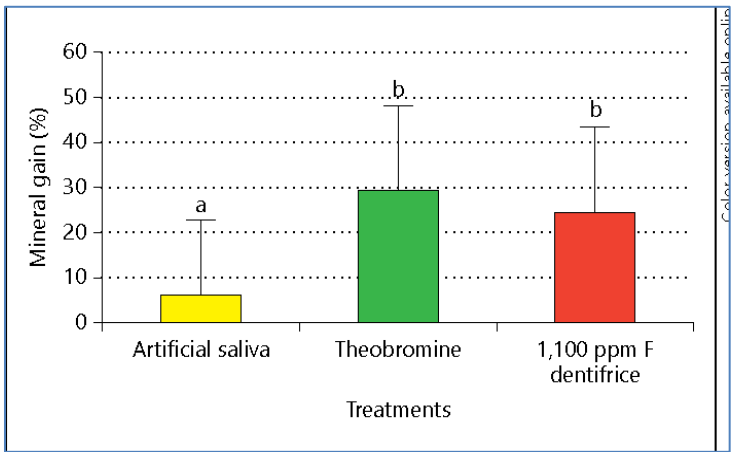

Fig. 1. Relation of mineral gain (%) with theobromine, artificial saliva and fluoride dentifrice

1.4 Effect of Caffeine on Neonatal Teeth

A chance discovery was made while researching caffeine's effect on developing teeth. Teeth are made up of hydroxylapatite (HAP). Caffeine's presence in beverages and pharmaceuticals is common in our everyday lives; nevertheless, caffeine's effects on growing teeth have received insufficient consideration. Caffeine diffuses in human breast milk, and when the maternal diet was supplemented with caffeine, the neonate ingested caffeine through the milk. It has been discovered that, caffeine consumption resulted in the generation of small crystals of hydroxylapatite in the developing teeth. When enamel specimens were exposed to acidic solutions in vitro, liberation of calcium and phosphorus ions was seen from the enamel surface. Furthermore, an animal research also supported the hypothesis that smaller HAP crystallites was associated to a higher rate of dental caries. However, theobromine (3, 7-dimethylxanthine), a caffeine-like compound, promoted the development of bigger HAP crystallites. The intake of theobromine by breastfeeding dams showed a reduced release of phosphorus, magnesium and calcium ions from the enamel surface in the emerging teeth of neonates in vivo. Therefore crystallites are smaller in acid susceptible teeth rather than in acid resistant teeth. This suggested that, in early neonatal period, when teeth are unveil to caffeine would easily dissolve and leads to caries susceptible teeth in future. Maternal diet should be supplemented with theobromine instead of caffeine [24,25].

1.5 Theobromine as a Better Alternative to Fluorides

Fluorides are commonly used as chemotherapeutic agent for dentinal hypersensitivity as it is quite inexpensive and can be administered through variety of cost effective methods. Fluoride based toothpaste has been standard for many years. Some of the commercially available fluoride containing toothpastes are ‘Colgate Cavity Protection Toothpaste’ Active ingredient of this toothpaste is sodium monfluorophosphate, 0.76%; ‘Crest Gum Detoxify’ active ingredient is stannous fluoride, 0.454%; ‘Sensodyne Proenamel Gentle Whitening Toothpaste’ active ingredient is sodium fluoride, 0.15% and potassium nitrate 5%. Although being a gold standard in oral care, it has many detrimental effects. In the developing period of teeth, exposure to high levels of fluoride can result in dental fluorosis. It is also recommended that, children below 6 years of age should not use mouthwash containing fluoride. There may be risk of permanent discolouration of teeth in developing period on ingestion of excessive fluoride [26]. Excess intake of fluoride also has harmful effect on bones known as skeletal fluorosis. Bones become less elastic and hardened [27]. Fluoride can cause osteosarcoma in boys [28]. A modern report from china suggested, excessive intake of fluoride can lower IQ level of a child [29]. A recent report suggests that intake of fluoride is interlinked to thyroid gland disease. Fluoride in excess can harm the parathyroid gland. Hyperparathyroidism, or the unregulated production of parathyroid hormones, can develop as a result of this [30, 31].

Recommended fluoride consumption: 0.05-0.07 mg/kg/day.

Probable toxic dose: 5mg/kg

Certain lethal dose: 32-64 mg/kg

1.6 Various Researches on Theobromine

1] A pilot study was undertaken by Kargul B, Zcan M, Peker S, Nakamoto T, Simmons WB, Falster AU, and others. The purpose of this study was to see how theobromine altered the surface hardness and topography of human enamel at two distinct doses. Prior to the experiments, with 0.1 percent thymol solution at room temperature, twenty four newly extricated third molars of human were gathered and kept in purified water. For about 5 minutes, a layer of theobromine is applied on enamel specimens, of 100 mg/l or 200 mg/l doses in purified water. No theobromine was received to the enamel specimens on the control group. Then these were kept for about one week in distilled water and underwent SEM investigation. In acidic hydroxyethyl cellulose, these specimens got demineralised after three days. Following micro hardness measurements, they were then incubated for 5 minutes in 100 or 200 mg/l theobromine. The distilled or purified water was used to keep the control group. The specimens were washed in distilled water before being immersed in remineralizing solution for next 18 hours. Before artificial demineralisation, every specimen's micro hardness of the enamel surface was measured. After demineralization, study group specimens were developed in either 100 or 200 mg of theobromine, while the untreated group ones was maintained in

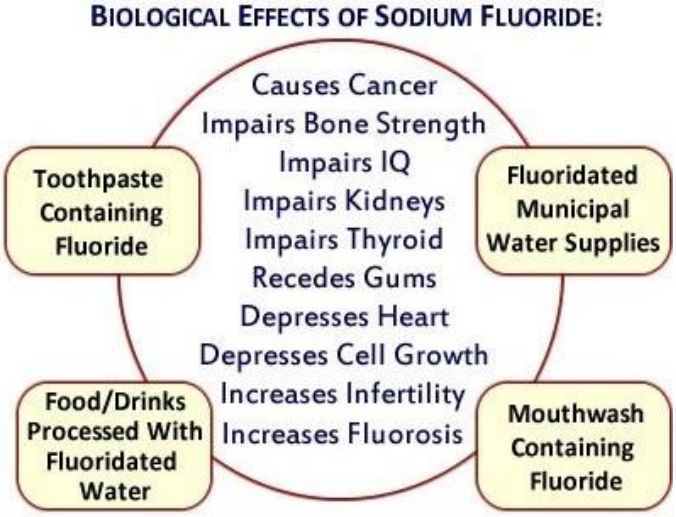

Fig. 2. Fluoride toxicity

remineralisation solution. According to the findings, enamel surfaces of untreated group specimens had pits and smooth hummocky surface on it. Study group specimens differed in their responses to the two concentrations. The group that was exposed to a 200 mg/l solution for 5 minutes had more globules on their enamel than the group that was exposed to a 100 mg/l solution [32]. According to the findings, it was discovered that the enamel surface was protected using theobromine as a stimulant.

Amaechi BT, Mathews SM, Mensinkai PK et.al, [2] conducted a study on Effect of theobromine containing toothpaste on dentinal tubule occlusion. The goal of this study was to see if toothpaste containing theobromine, both with and without fluoride, has the capacity to occlude dentinal tubules. For about seven days, four intraoral appliances with dentin blocks were wore by 80 participants where one of the four test dentifrices was used. The four test dentifrices were (theodent—classic—FR), (theodant—classic—R), (colgateR regular), (sensodyneR—5000—Nupro). The four appliances were removed in the order of one, two, three and seven days. Scanning Electron Microscopy was used to examine treated and untreated blocks. Effectiveness of each dentifrices were compared based on DSL%; FOT%; POT% and COT%. This gave an estimation of percentage of tubules in treated and untreated blocks. Scanning electron microscopy showed increase in COT% and DSL%. After 1 to 2 days, Theodent-classic® (TC) and Theodent-classic®-F (TCF) had significantly higher ($p<0.05$) COT than Colgate and sensodyne. After 3 and 7 days, the lower COT% ($p<0.05$) was seen in Colgate than these three. Except for Colgate, the percentage COT increased within each dentifrice. According to the findings, TC, TCF, and Sensodyne had significantly ($p<0.05$) higher DSL% than Colgate. This study suggested that toothpastes containing theobromine, both with and without fluoride were likewise more efficient than novamin®-containing toothpaste in terms of dentin tubule occlusion and smear layer deposition [33].

2. CONCLUSIONS

Fluorides have been used as a preventive measure for dental caries for many decades, but they have some drawbacks such as toxicity, fluorosis, and so on. The antifluoride lobby has raised concerns about the use of fluorides. This is the time to experiment with new formulations and techniques that are both non-hazardous and extremely useful.

Theodent 300 toothpaste is the commercially available product that contains theobromine. Theodent toothpaste harness the power of cocoa. Rennou, the main component in Theodent, is a unique compound that combines theobromine, calcium, and phosphate to enhance enamel remineralization. Despite its power, it is also nontoxic, not harmful if swallowed and safe for paediatric use.

The strength of evidence for its effectiveness against the gold standard, fluoride, is promising, but due to a lack of clinical trials, it is not being used. If this proves to be beneficial and cost effective in the future, it may usher in a new era

of prevention. There is an absolute need for more clinical trials to carry on theobromine's benefit in caries-preventive products and also oral hygiene.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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