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## CPP-ACP complex as a solution to the problem of complications after teeth bleaching - a literature review

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### Abstract:

Introductions and purpose: Teeth bleaching is an increasingly popular procedure that comes with its specific set of complications including damaged enamel, dentin hypersensitivity and increased vulnerability to bacterial colonization. CPP-ACP complex possesses remineralizing and bacteriostatic properties as well as the ability to abolish dentin hypersensitivity. The aim

of this study is to systematise the state of current knowledge on the use of casein phosphopeptide with amorphous calcium phosphate in combating complications after tooth bleaching.

Description of the state of knowledge: The CPP-ACP complex used alone or in a protocol with a bleaching agent, in a way that is comparable to other products, abolishes post-operative dentin hypersensitivity by blocking the flow of dentino-pulpal tubular fluid. It restores the morphological properties of the tooth, by increasing the hardness of the bleached enamel, more effectively than fluoride agents. Casein phosphopeptide with amorphous calcium phosphate limits the penetration of the bleaching agent into the tooth chamber, thereby preventing the development of pulp inflammation. Moreover, because of its buffering properties, it prevents the development of caries on surfaces weakened by the bleaching process.

Summary: Casein phosphopeptide with amorphous calcium phosphate is undoubtedly a useful compound in combating complications after teeth bleaching - it combats dentin hypersensitivity, and given its very strong buffering, remineralizing and enamel-strengthening properties, as well as its lack of toxicity - it should become a permanent element of equipment in every dental office.

Keywords: tooth bleaching; casein phosphopeptide-amorphous calcium phosphate; dentin sensitivity

### **Introductions and purpose:**

In the 21st century, people are under constant pressure created by the media which create an illusory image of beauty, making society constantly strive for artificially created perfection. As a result, patients are increasingly opting for teeth bleaching procedures, which, apart from indisputable advantages, bring numerous complications, such as damage to the enamel, weakening of the periodontal structures, and dentin hypersensitivity, with the latter becoming an increasingly more frequent issue in dental offices. [1]

Dentin hypersensitivity is defined as short, acute pain, the source of which, according to the most widely accepted hydrodynamic theory by Brännström, is the movement of the fluid inside the dentinal tubules. That movement causes irritation of the nerve endings present in the pulp. [2] The pain reaction is caused by a stimulus that is harmless to a healthy tooth, and according to studies, the cold stimuli are the most frequent causes of increased dentin

reaction.[3] There are numerous causes of hypersensitivity, such as all sorts of enamel cracks, leaky fillings, carious, erosive and abfractional lesions, but also severe gum recession, or diet rich in low pH products.[4] Bleaching agents are also a significant contributor in causing dentin hypersensitivity - according to several authors, it is the post-treatment hypersensitivity that is the main adverse effect linked with the tooth bleaching process.[5] A study conducted by Jorgensen i Carroll in 2002 showed that around 50% of patients who have had their tooth bleached experienced post-treatment hypersensitivity.[6] These conclusions were further confirmed by, i.a. Javier Martin in 2013, whose analysis showed an increased reaction of dentin in all examined patients, who have undergone the teeth bleaching in-office.[7] However it should be remembered that dentin hypersensitivity is caused by all other forms of the bleaching procedures as well, and mainly depends on the concentration of the bleaching substance.[8] Such increased reaction of the dentin is caused by the infiltration of bleaching agent, such as hydrogen peroxide or carbamide peroxide, into the tooth chamber, and later on, irritation of the pulp. As a consequence the pulp is transiently inflamed. [9] Main target of treating hypersensitivity is to block the mechanisms upon which the hydrodynamic theory is founded. The main course of action here is to block the dentinal tubules by creation of insoluble complexes and interrupting the nerve response to the pain stimuli through the use of the products containing ionized potassium.[1] Among options of treatment we can distinguish invasive methods, such as glass-ionomere or composite fillings, endodontic treatment of a hypersensitive tooth, or soft tissue transplant. Non-invasive methods include, for example, products containing arginine and calcium carbinade; potassium and fluoride ions; calcium, strontium, and oxalate compounds.[8] Non-invasive methos also include the use of casein phosphopeptide with amorphous calcium phosphate – CPP-ACP.[10]

Dentin hypersensitivity is becoming a more frequent and serious issue, more frequent and serious one than many dentists believe.[11] Pain causes intense discomfort, and that caused by teeth bleaching may become so severe, that it forces patients to terminate the treatment – that is why every patient should be examined in terms of hypersensitivity risks before starting teeth bleaching.[12]

Besides hypersensitivity, tooth bleaching is also responsible for weakening of the enamel structure. Observations following usage of tooth bleaching agents which contain carbamide peroxide in various concentrations, proved a 7,7% decrease in the microhardness of the enamel, compared to the initial hardness. Moreover, tooth bleaching procedure is considered to be harmful not only to the enamel, but to the dentin as well. Increased bacterial

adhesion to dental fillings after teeth bleaching has also been proven.[13-14] Some hope is offered by new, innovative solutions, such as combining bleaching agents with substances that show remineralizing properties. A special role may be played by CPP-ACP which when applied during tooth bleaching procedure increases enamel microhardness, as well as reduces the infiltration of hydrogen peroxide towards the tooth chamber.[14]

The purpose of this article is to systematise the current state of knowledge on the use of casein phosphopeptide with amorphous calcium phosphate in the control of the complications after tooth bleaching.

Could CPP-ACP complex provide the solution to dentin hypersensitivity, the increased risk of caries, and the enamel microdamage caused by tooth bleaching?

### **Description of the state of knowledge:**

Casein phosphopeptide with amorphous calcium phosphate is a product that has already found its use in dentistry. CPP-ACP is a nanocomplex consisting of phosphopeptide casein protein (CPP) and phosphorylated serine and glutamic amino acid residues.[15] In addition, it contains a precursor to dental hydroxyapatite, namely amorphous calcium phosphate (ACP), whose ions are phosphorylated by serine residues present in CPP.[16] Above all, it is a substance associated with remineralizing effects and the prevention of carious lesions.[17-19] Remineralization is caused by the stabilisation of calcium and phosphate ions present in solution, through the binding of ACP to the amino residues of the phosphorylated serine present in CPP. Regular use of products with CPP-ACP complex results in saturation of ions in saliva and biofilm, making them available for subsequent precipitation as amorphous calcium phosphate, which promotes tooth remineralization.[20] Moreover, the CPP-ACP complex also has the property of reducing dentin hypersensitivity - calcium and phosphate ions precipitated from amorphous calcium phosphate (ACP) diffuse through previously phosphorylated fibrils of exposed dentin intercalated collagen, which promotes the formation of hydroxyapatite.[21] The complexes formed within the tubules partially block the flow of dentino-pulpal fluid, which, according to hydrodynamic theory, reduces dentin hypersensitivity.[22] By partially blocking the dentinal tubules, the CPP-ACP complex mimics, among others, the calcium arginine-carbonate complex, or strontium acetate in its effects; however, it should be remembered that the compound is relatively easily neutralized by vigorous tooth brushing or a diet rich in low pH products, so repeated application of the product is necessary.[23-25]

The first and most important complication after teeth whitening is dentin hypersensitivity. After treatment with peroxide-containing agents, the exposure of dentin to the oral environment does not always happen, as in the case of, for example, erosion or abfraction cavities. Consequently, the pain has a different etiology and a synergistic effect of therapy is necessary to improve the patient's condition during aesthetic treatment.[26] For many years, studies have been conducted that analyze the direct effect of CPP-ACP complex on hyperreactive dentin after teeth whitening; in addition, many studies have sought to compare its effects and efficacy with other compounds used to treat tooth sensitivity. A 2019 study showed that the use of CPP-ACP after at-home teeth whitening with 20% carbamide peroxide was beneficial in terms of reducing dentin hypersensitivity. In addition, the complex had no effect on the color of the teeth obtained during the whitening procedure.[27] A similar experiment was conducted in 2018 by Oldoini and Bruno, who tested the effectiveness of the complex alone and in mixing with carbamide peroxide. They showed that patients receiving ACP in the bleaching mixture experienced reduced tooth sensitivity (\* $p \leq 0.05$ ). Patients receiving the complex during at-home treatments showed a statistically significant (\*\*\*) $p \leq 0.0001$ ) reduction in tooth sensitivity.[28] Subsequent studies confirmed the fact that the use of a mixture consisting of a compound with whitening properties and the CPP-ACP complex results in a reduction of dentin hypersensitivity.[29-31] The results of studies comparing the efficacy of individual substances are not clear-cut; a 2016 study showed a comparable hypersensitivity lifting efficacy of casein phosphopeptide with amorphous calcium phosphate (CPP-ACP), and a mixture of potassium nitrate 5% with sodium monofluorophosphate 0.7%.[32] Sodium fluoride 2%, compared to CPP-ACP 10% complex, also shows similar efficacy - both in terms of eliminating hypersensitivity, as well as in stabilizing the colour after bleaching.[33] In 2017, the efficacy of phosphopeptide with fluoride and calcium-sodium phosphosilicate (NovaMin) was compared, and significantly better results were obtained this time with CPP-ACP.[34]

Teeth hypersensitivity after whitening is the result of the penetration of molecules of the whitening substance through the enamel and dentin into the pulp, where they cause a reversible inflammation of the pulp, resulting in an increased pain response to thermal stimuli such as cold.[35] Research on this process was conducted in 2020, and showed that a bleaching protocol based on a mixture of CPP-ACP and bleaching gel reduces the penetration of hydrogen peroxide (35%), and thus no damage to the pulp occurs. In addition, the mixture maintains the effectiveness of bleaching.[36]

Tooth whitening is also linked to quite significant damage to the enamel - among other things, dissolution of calcium compounds, increased porosity and penetration of harmful acids deep into the tooth tissues are observed.[13, 37] Casein phosphopeptide with amorphous calcium phosphate is a compound primarily characterised by its remineralizing activity. An experiment conducted in 2018 by applying the complex to previously whitened teeth with 35% hydrogen peroxide for 7 consecutive days showed following results - a significant increase in the thickness of the structure and calcium content was observed, the separation and fragmentation index on the outer surface of the enamel decreased, and a covering layer appeared around the enamel prisms after 7 days. In addition, the spaces between hydroxyapatite crystals decreased. The clinical impact of the abovementioned study is significant: CPP-ACP neutralizes any adverse complications on the enamel surface and minimizes the side effects of the whitening procedure.[38] Other studies also confirm the significant enhancing effect of CCP-ACP used alone on whitened enamel, regardless of whitening method and product concentration.[39-42] Reduced porosity and increased, or comparable to the pre-whitening state, tooth hardness were also observed by applying mixtures of various whitening substances, including hydrogen peroxide (10% and 35%) or carbamide peroxide (10%,16%, 36%) along with the CPP-ACP complex.. These mixtures were used in different protocols - before, after and during bleaching, with comparable results. Scanning electron microscopy used in some studies has shown that the increased microhardness of enamel is caused by the mineral buildup on the surface of bleached enamel. [43-45] A comparative study of the effects of fluoridated products and CPP-ACP on the enamel bleached by a 35% hydrogen peroxide solution was conducted in 2009 and 2016. The experiments showed that all products restored the enamel surface morphology; however, CPP-ACP showed the highest efficacy.[46,47]

Surfaces on which the whitening agent has acted, such as dental fillings, are more susceptible to bacterial colonization.[13] Bearing in mind the weakened enamel as well - the teeth whitening process can contribute, in the presence of certain factors, to the development of the carious process. Casein phosphopeptide with amorphous calcium phosphate has a buffering capacity to prevent the significant pH reduction that occurs during the growth of acidogenic bacteria.[48] As a result, CPP-ACP slows the growth and reduces the number of bacteria with high cariesogenic potential, as for example *Streptococcus mutans*.[49-50]

## **Summary:**

Casein phosphopeptide with amorphous calcium phosphate is undoubtedly a useful compound in dealing with post-tooth bleaching complications. Used alone or in mixtures with whitening substances, it reduces dentin hypersensitivity by blocking the flow of dentino-pulpal fluid. In addition, it strengthens weakened enamel by depositing lost minerals on its surface, and, compared to fluoridated agents, it rebuilds the morphology of the whitened tooth tissues more effectively. Casein phosphopeptide with amorphous calcium phosphate used in the protocol reduces the penetration of the bleaching agent into the tooth chamber, thereby preventing the development of pulp inflammation. The CPP-ACP complex also has a buffering effect, which reduces the probability of caries development on the tooth surfaces weakened by the bleaching procedure.

To sum up, casein phosphopeptide with amorphous calcium phosphate is a competitive compound for other hypersensitivity fighting agents, and due to its very strong buffering, remineralizing and enamel-strengthening properties, as well as its lack of toxicity - it should become a permanent element of equipment in every dental office.

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