

# CPP-ACP in the Treatment of Hyper Sensitivity Associated with Vital Tooth Bleaching: A Systematic Review

Pratyusha Giri  
Undergraduate student,  
SRM dental college, Ramapuram, Chennai, India

Sathyapriya S, Sindhu R., Bharathwaj V. V.  
Senior Lecturer, Department of Public Health Dentistry,  
SRM dental college, Ramapuram, Chennai, India

Dinesh Dhamodhar, Rajmohan M  
Reader, Department of Public Health Dentistry,  
SRM dental college, Ramapuram, Chennai, India

Elakiya S  
Postgraduate student,  
Department of Public Health Dentistry,  
SRM dental college, Ramapuram, Chennai, India

Prabu D  
Professor and Head of the Department,  
Department of Public Health Dentistry,  
SRM dental college, Ramapuram, Chennai, India

**Abstract:-** Hypersensitivity is the most common adverse effect of vital tooth bleaching. To overcome this, a lot of desensitising agents are introduced. casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) is a milk-derived complex that causes demineralisation of tooth structure. To assess the efficacy of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) in treating the hypersensitivity associated with vital tooth bleaching. A systematic review was performed using electronic databases like PubMed, science direct, Wiley online library, lilacs and google scholar using certain keywords. Out of 265 articles, five articles were related to the research topic. The review is described according to the PRISMA guidelines. CPP-ACP is more effective in the treatment of sensitive teeth with vital tooth bleaching. The study concludes that casein phosphopeptide-amorphous calcium phosphate complex (CPP-ACP) has the ability to reduce the post-operative sensitivity caused by at-home and in-office vital tooth bleaching without affecting the colour stability of the bleached tooth.

**Keywords:-** CPP-ACP, Hypersensitivity, vital tooth bleaching, at-home bleaching, in-office bleaching.

## I. INTRODUCTION

Vital tooth bleaching is an advanced treatment option to treat discolouration of teeth without affecting the tooth vitality [1]. According to American Dental Association (ADA), bleaching is a treatment involving oxidative chemical that increases the value of teeth by altering reflection/ absorbing the tooth structure. The Desire for a flawless smile with minimum intervention has widened the scope of vital tooth bleaching [2]. Vital bleaching can be done in patients with mild fluorosis and tetracycline stains or to match the crown's colour that is lighter than the natural teeth.

However, it is contraindicated in patients with severe enamel loss, hypersensitivity, children with large pulp chambers, exposed root surface, dental caries etc.

Vital tooth bleaching with peroxides has become the most popular treatment regimen to brighten the discoloured teeth [3]. The spectrum of vital bleaching ranges from dentist-supervised in-office bleaching and dentist prescribed at-home bleaching to over-the-counter consumer-available systems.

In-office bleaching is usually done with 35% hydrogen peroxide solution by placing it on the teeth followed by the application of heat. These bleaching agents are commercially available in gel, which prevents the running of material on application. Before application of the gel, it is important to protect the gingival tissues with Vaseline and isolate the teeth with a rubber dam. The gel is activated by application of heat. Hence it is known as thermocatalytic bleaching. The entire treatment time should be less than 30 minutes.

For at-home bleaching usually 10% carbamide peroxide is used with custom-fit trays. It is important to clean the teeth surface before application of the bleaching agent. The tray should be worn for a time period of 4 hours. The tooth surface and the trays should be thoroughly cleaned followed by the application.

These bleaching agents contain peroxides which are oxidative agents that produces unstable free radicals as a result of oxidation-reduction reaction that penetrates into interprismatic area of enamel and breaks down complex macromolecules into smaller molecules that reflects the light more, and the tooth appears whiter [4].

However, vital tooth bleaching shows adverse effects like tooth sensitivity and increase of enamel porosity. In enamel, it reduces the microhardness. A lot of In vitro studies have shown that peroxide penetrates the enamel dentin and enters the pulp. Due to the lower pH of the bleaching solution causes demineralisation of enamel and

dentin and irritates the pulp, causing reversible pulpitis and producing tooth sensitivity [5].

Recently a lot of re-mineralising agents have been introduced to reduce the tooth sensitivity followed by vital bleaching. Casein phosphopeptide-amorphous calcium phosphate (CPP- ACP) was first postulated in 1998. These are nanocomplexes that are derived from bovine milk protein. CCP-ACP has anti-cariogenic property.

CCP has the ability to localise ACP at the tooth surface. It increases the calcium phosphate level in plaque. Casein phosphate maintains the supersaturation of saliva by providing a pool of calcium and phosphate by forming nanoclusters with amorphous calcium phosphate [6].

CPP-ACP provides a higher safety level as it is a unique milk-derived protein [7].

Previous systematic reviews have assessed the remineralisation property of the CPP -ACP on the demineralised tooth surface. The aim of this systematic review is to assess the effect of CPP-ACP on tooth hypersensitivity followed by vital bleaching. To evaluate the efficacy of CPP-ACP on tooth sensitivity followed by vital bleaching.

*E. Search Database*

S.NO.	DATABASES	SEARCH WORDS	NUMBER OF ARTICLES
1.	GOOGLE SCHOLAR	CPP-ACP AND tooth hypersensitivity AND vital tooth bleaching AND efficacy	198
2.	PUBMED	Vital tooth bleaching AND CPP-ACP AND dentin hypersensitivity	2
3.	COCHRANE	CPP-ACP AND Vital tooth bleaching	2
4.	MEDLINE	CPP-ACP AND vital tooth bleaching AND teeth hypersensitivity (in advanced search under key words)	0
5.	LILACS	Tooth hypersensitivity AND Vital tooth bleaching AND CPP-ACP	0
6.	WILEY	Vital bleaching AND hypersensitivity AND CPP-ACP (searched under title abstract subject)	27
7.	SCIENCE DIRECT	Dentin hypersensitivity AND CPP-ACP AND vital tooth bleaching	36

Table 1

**II. MATERIALS AND METHODS**

*A. Study design:*

A systematic review of randomised control trials done on the efficacy of CPP- ACP on tooth sensitivity followed by vital tooth bleaching.

*B. Eligibility criteria:*

- a) Inclusion criteria
  - Articles showing the efficacy of CPP-ACP on tooth sensitivity followed by vital bleaching.
  - Articles in English.
  - Randomised control trials.
  - Originalarticles.
  - Full textarticles.
- b) Exclusion criteria-
  - Articles without full text.
  - Articles in different languages.
  - Articles with only abstracts.
  - Editorials.

*C. Search strategy:*

Articles related to efficacy of CPP-ACP on tooth sensitivity followed by vital tooth bleaching was thoroughly searched in databases like Google Scholar, PubMed, Ovid, Science Direct, Lilacs, Wiley, Cochrane. The MeSH terms were "CPP-ACP", "tooth sensitivity", "vital tooth bleaching" using AND

*D. Search Engines:*

- The search engines were used –
- GoogleScholar
  - PubMed
  - Ovid
  - Science Direct
  - Lilacs
  - Wiley
  - Cochrane

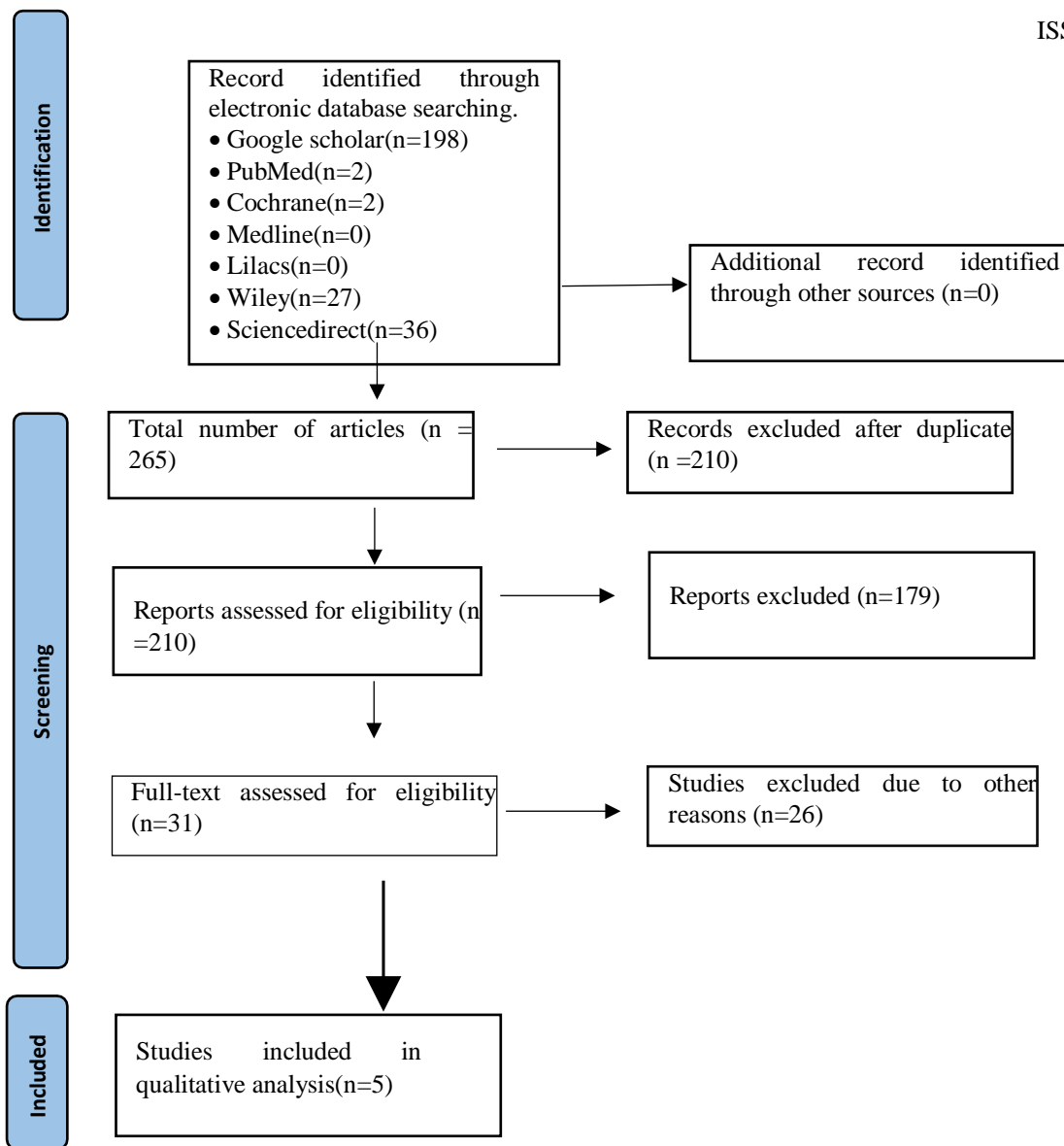


Fig. 1: Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review

### III. RESULTS

S. No.	Author and year of publication	Type of study	Materials and sample size	Parameters	Methodology	
					Pre- experimental interventions	Experimental interventions
1.	Oula Yassin <sup>8</sup> (2018)	Double-blinded randomised control trial	Twenty-four people were randomly divided into two groups. n=12(Placebo)	Toothsensitivity is recorded using the visual analogue scale (VAS)ranked from '0' no sensitivity to '10' severe sensitivity.	Participants were provided with a syringe containing 20% carbamide peroxide gel along with vacuum compressed custom trays and instructed to use the bleaching gel four/day.	Participants were provided with a white colour coded container either with placebo gel or CPP-ACP and asked to apply it for 30 minutes once a day followed by the bleaching procedure for seven days.
2.	Burak GÜMÜŞTAŞ <sup>9</sup> (2021)	Triple blinded randomised control trial	Sixty-four subjects were randomly allocated into four groups.	Tooth sensitivity is recorded using the visual analogue scale (VAS) and		Participants were divided into 4 groups and each group was treated with placebo, ACP- CPP, Nano

			n=16 group A n=16 group B n=16 group C n=16 group D	calculated at four levels: 0= None 1=Mild 2=Moderate 3=Considerable 4=Severe		hydroxyapatite(n- HAP) and neutral sodium fluoride (NSF) respectively for 4 minutes. Bleaching was done using 38% hydrogen peroxide activated by light for 45 minutes in 3 intervals. (15 minutes each)
3.	GA Maghaireh <sup>10</sup> (2014)	Randomised control trial	51 participants were randomly allocated in 3 groups. n=17 (Placebo) n=17(2% sodium fluoride) n=17(10% CPP-ACP)	All the participants were provided with a sensitivity sheet to record the post bleaching sensitivity with a visual analogue scale ranging from 1-10. 0=none 1-3=mild 4-6=moderate 7-10=severe	35% hydrogen peroxide gel was applied on the tooth surface of the maxillary anterior teeth for 15 minutes. The agent was washed and washed away every 15 minutes during a 45 minutes application. The whitening agent was removed with cotton roll and the gingival barrier was removed. Teeth were rinsed thoroughly and post-whitening shade was determined.	Participants were divided into 3 groups of 17 individuals. A small amount of gel applied on the labial surface of teeth from unmarked syringes containing gel without desensitising agent, gel with 2% sodium fluoride and gel with 10% CPP-ACP. The gel was undisturbed for 3 minutes. After that, the participants were asked to expectorate thoroughly and asked not to eat, drink and rinse after half an hour. Participants were instructed to use the assigned gel twice daily after brushing their teeth.
4	Shaista Rashid <sup>11</sup> (2021)	Randomised, controlled, split-mouth crossover design clinical trial.	32 individuals were randomly allocated into two groups (n=16) Group 1: control arch= maxilla Intervention arch =mandible Group 2: Control arch=mandible Intervention arch =maxilla.	Tooth sensitivity was measured with a visual analogue scale ranging from 0(no sensitivity) to 10(severe sensitivity).	Participants were instructed to use 15% carbamide peroxide gel with a custom scalloped tray after brushing and flossing their teeth. Group 1 is instructed to bleach the maxillary arch and group 2 is instructed to bleach the mandibular arch for 6-8 hours at night for two weeks.	After two weeks, participants are asked to apply the bleaching agent with MI (minimal intervention)paste. Group 1 was instructed to use bleach and MI paste in the mandibular arch and Group 2 was instructed to use it in the maxillary arch. Participants were asked to use the non-scalloped tray with MI paste for 5 minutes after brushing and flossing, followed by application of bleaching agent for 6-8 hours at night for two weeks
5	Manjot Singh <sup>12</sup> (2017)	Randomised control trial	45 individuals are randomly allocated into 3 groups. Group 1: Placebo(n=15)	Tooth sensitivity was recorded using a visual analogue scale for 14 days. 0=none 1-3=mild	Pre bleaching shades were determined. The experimental teeth were isolated with a light cure resin	45 individuals were divided into 3 groups. group 1 received the treatment with placebo gel, group 2 was given cream with 1.1%

			Group 2: Cream with 1,1% sodium fluoride Group 3: Cream with 10% CPP-ACP.	4-6= moderate 7-10=severe	dam. The bleaching agent was applied on the maxillary tooth surface in 2 intervals for 20 minutes in total 40 minutes duration and postbleaching	sodium fluoride and group 3 was given cream with 10% CPP- ACP. A pea-sized amount of the desensitising agents was applied on the labial surface of the tooth
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Table 1: Characteristic of included studies and methodology

Sl. no	Author and Year of publication	Outcome Assessment	P-value	Notes
1.	Oula Yassin <sup>8</sup> (2018)	Patients treated with CPP-ACP followed by bleaching has shown significant reduction in tooth sensitivity on 3 <sup>rd</sup> and 7 <sup>th</sup> day than the control group.	P=0.002	There was no deteriorating effect on colour change when compared with placebo.
2.	Burak GÜMÜŞTAŞ <sup>9</sup> (2021)	Control and CPP-ACP showed significantly higher tooth hypersensitivity than NSF and n-HAP. CPP-ACP shows reduction in tooth hypersensitivity than placebo but there was significant difference with NSF and n-HAP.	P<000.8	There was no significant color alteration of the teeth on application of remineralising agents.
3.	GA Maghaireh <sup>10</sup> (2014)	The participants of the placebo group experienced sensitivity over 14days. The participants of CPP-ACP group had sensitivity up to 4th day and the fluoride group showed presence of sensitivity up to 10 days.	Day 1;p=0.112 Day 2;p=0.532	The participants with fluoride have better colour stability than CPP-ACP.
4.	Shaista Rashid <sup>11</sup> (2021)	At baseline: No significant difference in test and control groups. After treatment: The thermal sensitivity score was greater in bleaching without MI paste than with MI paste. 2weeks: There was no significant difference in tooth sensitivity for both the groups. During a period of 14 days, the test group showed lower tooth sensitivity than the control group.	P=0.063  P=0.011  P=0.214  P=0.002	There is no significant shade change occurred in the test and control subjects.
5.	Manjot Singh <sup>12</sup> (2017)	There was a significant difference between group 1 and group 2 and 3. There was no significant difference between group 2 and 3.	Group 1= 0.1  Group 2= 0.001  Group 3=0.001	There is no significant difference in shades change in all 3 groups.

Table 2: Outcome assessment and result

S. No	Author and year of publication	Random sequence generation	Allocation concealment	Selective reporting	Other source of bias	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data
1.	Oula Yassin <sup>8</sup> (2018)	+	?	+	?	+	+	?
2.	Burak GÜMÜŞTAŞ <sup>9</sup> (2021)	?	+	-	+	+	+	+
3.	GA Maghaireh <sup>10</sup> (2014)	?	?	?	+	?	?	+
4.	Shaista Rashid <sup>11</sup> (2021)	+	+	+	+	+	+	+
5.	Manjot Singh <sup>12</sup> (2017)	?	?	+	?	+	+	+

Table 3: Assessment of risk of bias in included studies

+ =Low risk; -=High risk; ? = Unclear

#### IV. DISCUSSION

The systematic review yielded 265 articles screened for duplicates and eligibility criteria, and five final articles were selected to be included in this study.

The aim of this study is to evaluate the efficacy of CPP-ACP on tooth sensitivity followed by vital tooth bleaching. The results from 5 articles reveal that CPP-ACP causes reduction in the tooth sensitivity caused due to vital bleaching.

Oula Yassin [8] conducted a double-blinded randomised control trial that shows there was increased surface roughness due to the use of 20% carbamide peroxide (at home) which caused increased tooth sensitivity due to penetration of bleaching agent into the pulp chamber. Use of CPP-ACP increases the mineral content and improves the microhardness of the enamel. Thus reduces the penetration of bleaching agent and reduces the tooth sensitivity.

The study by Burak gümüştas [9] has included 3 remineralising agents to compare the tooth sensitivity by vital in-office tooth bleaching. 3 agents are CPP-ACP, Nano hydroxyapatite crystals (n-HAP) and neutral sodium fluoride (NSF). When compared, the experiment shows all the 3 agents has reduction in tooth sensitivity with placebo group. There was significantly higher tooth sensitivity in CPP-ACP than the other two groups. But when compared with placebo CPP-ACP showed a reduction in hypersensitivity.

In the study by GA Maghaireh [10] CPP-ACP and sodium fluoride were compared with the placebo group. The study showed there is reduction in tooth sensitivity in 4<sup>th</sup> day for CPP- ACP group and on 10<sup>th</sup> day for the sodium fluoride group. The intensity of pain was lower in sodium fluoride group when compared with CPP-ACP and the placebo group.

Shaista Rashid [11] conducted a split-mouth randomised control trial where one arch was used as control and the opposite arch as the test group. Immediately after treatment, there was a significant reduction in the tooth sensitivity of arch treated with CPP-ACP when compared with arch without mi paste. But there was no significant

difference between the test and control group after two weeks.

A study conducted by Manjot Singh [12] with 45 participants divided into 3 groups receiving treatment with CPP-ACP, sodium fluoride and placebo gel. The experiment shows there is a significant reduction in tooth sensitivity in CPP-ACP and sodium fluoride group when compared with the placebo group. There was a significant reduction in sensitivity on 3<sup>rd</sup> day in CPP-ACP and sodium fluoride group. The pain intensity was reduced to moderate level for both CPP-ACP and sodium fluoride but sodium fluoride showed the lowest intensity of pain.

All the 5 studies above have shown that the CPP-ACP causes reduction in tooth sensitivity after vital tooth bleaching. It is effective for both in-office, i.e., treatment with hydrogen peroxide as well as carbamide peroxide which is usually used as at-home bleaching agents.

The main advantage of vital tooth bleaching is rapid lightening of the shade of the tooth. It causes transient and intolerable sensitivity to the teeth [13]. According to some studies, the oxygen bubbles produced by the peroxides moves in the intratubular fluid and activates the interdental nerves and causes hypersensitivity [14]. To overcome this drawback desensitising agents are introduced to reduce the pain intensity due to hypersensitivity. CPP-ACP increases the concentration of calcium and promotes remineralisation of enamel by maintaining a supersaturated solution [15]. It causes the remineralisation of the enamel surface by filling the CPP-ACP in the enamel surface defects and makes the surface smoother stronger and reduces sensitivity. There are a lot of desensitising agents available. Mainly fluorides derivatives are used for post bleaching sensitivity which is equally effective as CPP-ACP. But fluoride occludes the dentinal tubules and reduces the hypersensitivity [16]. In the study conducted by Burak gümüştas [9] includes two material n-HAP and neural sodium fluoride. These two have better efficacy on post bleaching sensitivity than CPP-ACP. However, it is evident that CPP-ACP has a potential to reduce the pain intensity followed by vital tooth bleaching immediately or within 3 dayspost-application.

The above studies showed that there is a low risk of bias. Moreover, CPP-ACP is already proven to be effective on early carious lesion due to its remineralisation property.

Being a naturally occurring milk derivative product it can reduce the tooth sensitivity followed by at home and in-office vital tooth sensitivity. However, there is a difference in time and duration of application, randomisation, intervention methods, outcome assessment and blinding of the participants from which trial result can be affected.

## V. CONCLUSION

Within the limitation of this systematic review, there is sufficient evidence to conclude that casein phosphopeptide-amorphous calcium phosphate complex (CPP-ACP) has the ability to reduce the post-operative sensitivity caused by at-home and in-office vital tooth bleaching without affecting the colour stability of the bleached tooth.

## ACKNOWLEDGEMENT

Nil

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