Effects of 10,600nm carbon dioxide laser on remineralizing caries: a literature review

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Abstract

Purpose: To study the effects of carbon dioxide (CO_2) lasers (λ=10,600 nm) on remineralizing dental caries

Methods: This study involved performing a systematic search of the English articles archived in the PubMed, Scopus and Web of Science databases. The keywords used to identify the relevant articles were ((CO_2 laser) OR (carbon dioxide laser)) AND ((dental caries) OR (tooth remineralization)). Publications before 2019 were selected. The titles and abstracts of the initially identified articles were screened. Duplicate records, reviews and irrelevant studies were removed. Full texts were retrieved for publications that studied the effects of CO_2 lasers on remineralizing dental caries.

Results: The search identified 543 potentially relevant publications. A total of 285 duplicate records were removed. Sixteen articles were included in this review. Four studies reported that CO_2 lasers inhibited bacterial growth. The growth of cariogenic bacteria, mainly *Streptococcus mutans,* on an irradiated tooth surface was slower compared with non-irradiated ones. Four studies investigated the reduction of the demineralization of enamel with cariogenic challenge. They found that CO_2 lasers reduced the carbonate content of mineralized tissues and increased the microhardness of enamel. Nine studies used CO_2 lasers associated with topical fluorides in remineralizing dental caries. The results of the synergistic effect of laser irradiation and fluoride application with regard to the inhibition of caries progression varied among these studies, whereas laser irradiation could enhance fluoride uptake to demineralized mineral tissues.

Conclusion: 10,600nm CO_2 laser irradiation increased acid resistance and facilitated the fluoride uptake of caries-like lesions. In addition, it reduced the growth of cariogenic bacteria.

Keywords: carbon dioxide lasers; remineralization; dental caries; fluoride; review

Introduction

Dental caries, which was reported as the most prevalent oral condition in the Global Burden of Disease 2010 Study, remains a serious public health problem [1]. Approximately 3.9 billion people were affected by this oral condition [1], which exerted a substantial influence on individuals or communities with regard to pain and suffering, systemic health and quality of life [2]. Caries lesions were formed as a result of the dissolution of minerals from dental hard tissues, thus leaving a relatively porous tooth structure. Initial enamel caries lesions, constantly undergoing an everyday battle between progression and regression [3], developed during irregular periods of demineralization and remineralization. The development of cavities takes three to four years. Thus, sufficient time exists to interrupt this process by using various preventive and restorative strategies. Non-invasive or minimally invasive management strategies that take into account the dynamic process of caries lesions are treatment choices that focus on the preservation of tooth structures as much as possible [3]. These strategies may effectively inhibit or even entirely reverse the caries process. Conventional non-invasive management for caries inhibition includes oral health promotion, dental plaque reduction/removal and the use of fluoride tooth pastes or varnishes. Fluoride basically reduces the solubility of enamel and dentin and enhances the remineralization of tooth surfaces with early signs of mineral loss [4]. It has been suggested that caries progression may be remineralized when caries lesions are exposed to fluoride at levels of 0.095-0.190 ppm long term [5]. However, remineralization cannot be achieved with fluoride alone. The presence of calcium and phosphate ions is essential for remineralization to occur. When the salivary gland is not functioning properly, supplementing fluoride with calcium-based strategies, such as casein phosphopeptide amorphous calcium phosphate [6] and functionalized tri-calcium phosphate, may greatly assist remineralization. Another novel non-invasive approach is the use of laser irradiation on enamel or dentin in inhibiting caries progression.

Maiman developed the world's first laser, a ruby laser, in 1960 [7]. Four years later, in 1964 the first 10,600-nm carbon dioxide (CO_2) gas laser was developed [8]. Nitrogen and helium gases were added to the CO_2 laser tube to cool the laser gas, stabilize the electrical discharge process, increase pressure and transfer energy to the laser gas [9]. Unlike neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers (λ=1,064 nm) and argon lasers (λ=488-514 nm), enamel and dentin heavily absorb CO_2 lasers. CO_2 lasers are usually centered at 9,300, 9,600, 10,300 and 10,600 nm, respectively. CO_2 lasers emitting light at 9,300 and 9,600 nm have a higher absorption of hydroxyapatite than they do at 10,300 and 10,600 nm. However, a 10,600-nm CO_2 laser has been commonly used in medicine and dentistry, and most of the commercially available CO_2 lasers operate only at this wavelength. The effect of the irradiation of CO_2 lasers in caries research has been studied since the 1960s [10]. A number of studies investigated the potential of laser irradiation on enamel or dentin in remineralizing caries progression [11-15]. Studies reported that CO_2 laser irradiation had an inhibitory effect on demineralized mineral tissues. Moreover, it has been suggested that the combination of laser irradiation and topical fluorides had promising effects in remineralizing dental caries [16-18]. However, the effect of the caries remineralizing of CO_2 lasers remains to be elucidated. A literature search in PubMed and Scopus found no comprehensive review evaluating studies investigating the effects of the actions of CO_2 lasers in caries remineralizing. Therefore, the objective of this paper is to review the evidence regarding the effects of CO_2 lasers (λ=10,600 nm) on remineralizing dental caries.

Methods

Search strategy

Two investigators (KL and ISZ) performed a systematic search of the articles archived in three databases: PubMed, Scopus and Web of Science databases. The following keywords were used to identify the relevant articles: ((CO_2 laser) OR (carbon dioxide laser)) AND ((dental caries) OR (tooth remineralization)). The last search was performed in Jan 31, 2019. Publications before 2019 were chosen. A list of potentially eligible articles was developed, including publications searched using the keywords (Figure 1).

Study selection and data extraction

The records identified from the database search were checked for duplication. The titles and abstracts from the list of potentially eligible articles were screened after the duplicate publications were removed. Articles that did not study the effects of CO_2 lasers on remineralizing dental caries were excluded after titles and abstracts were screened. The remaining articles were retrieved with full texts. The reference lists of all of the included articles were screened to identify all possible eligible studies. The inclusion criterion for selecting studies for this review was as follows: studies investigated the effects of the actions of CO_2 laser on remineralizing enamel and dentin caries, including its action on cariogenic bacteria and the combination effect with topical fluorides on caries progression. For the included papers, the following information was recorded: publication details (authors and years), methods, outcome assessments (various criteria for studying the remineralizing of caries: the reduction of carbonate content, lesion depth, microhardness, mineral loss, surface morphology and bacterial counts) and the main findings. Two authors discussed any disagreements on study inclusion or data extraction with the third author (OYY) until a consensus was reached.

Results

The initial literature search identified 543 potentially relevant articles (143 articles in PubMed, 221 articles in Scopus and 179 articles in Web of Science). A total of 285 duplicate records were removed (Figure 1). After the titles and abstracts were screened, 242 articles that were classified as literature reviews, case reports, non-English articles or other irrelevant studies were excluded. No additional relevant publications were found from the references of the selected papers. Finally, 16 articles were found to meet the inclusion criteria and were included in this review. Among these articles, four studies examined the action of CO_2 lasers on cariogenic bacteria (Table 1), four studies investigated the effect of CO_2 lasers on demineralized mineral tissues (Table 2) and nine studies investigated the effect of CO_2 lasers combined with topical fluorides on caries-like lesions (Table 3).

Actions of CO_2 lasers on cariogenic bacteria

Four studies of the included articles studied the actions of 10 600-nm CO_2 lasers on cariogenic bacteria [12,16-21]. The effects of CO_2 laser irradiation on bacterial viability, biofilm architecture and the gene expression of S. *mutans* were investigated in these studies. Confocal laser scanning microscopy (CLSM) showed that dead and live bacteria were found in the marginal area of the irradiated spot and that no visible bacteria were left in the center of the irradiation area [12]. The total number of bacteria (live and dead) was less in the irradiated enamel than in the non-irradiated areas, and the number of live bacteria was larger than that of the dead ones, which were concentrated in the middle layers of the biofilm in all samples [12]. Irradiated enamel had a higher dead/live ratio in the top and deep layers compared with the non-irradiated sample [12]. A colony-forming unit (CFU) confirmed less growth of bacteria in the irradiated group compared with the control group [20]. Another study [21] reported that little lethal effect (less than 10%) was shown when S. *mutans* biofilm samples were irradiated at a fluence of 31 J/cm^2 compared with non-irradiated ones, whereas more lethal effects were presented when samples were exposed to fluences of 70 (23% killing effect) and 144 J/cm^2 (30% killing effect). Scanning electron microscopy (SEM) image analysis revealed a clear thermal effect of CO_2 laser irradiation on S. *mutans* biofilm, and a crater pattern in the biofilm was created, resulting in biofilm removal with a melted enamel surface in the irradiated spot [12]. Assessments using quantitative real-time polymerase chain reaction (PCR) demonstrated that no significant difference in the gene expression (gtfB and gbpB) of S. *mutans* was found between laser-irradiated samples and non-irradiated ones [20]. However, another study [21] using deoxyribonucleic acid (DNA) microarray analysis reported that 46 genes in the laser-irradiated samples showed changes in the gene expression at sublethal energies (31 J/cm^2), and most of these genes were related to transport proteins and energy metabolism. Fifteen of these genes were up-regulated, whereas 31 were downregulated [21].

Actions of CO_2 lasers on demineralized mineral tissues

Four studies investigated the effects of 10, 600-nm CO_2 lasers on the chemical and morphological changes of demineralized enamel, as well as on the inhibition of caries—for example, lesion progression. With respect to chemical changes, Fourier transform Raman spectroscopy showed a statistically significant reduction of carbonate content in irradiated enamel compared with non-irradiated and sound enamel [11]. This was consistent with the findings of another study that reported an approximately 40% loss of carbonate in the irradiated enamel using Fourier transform infrared spectroscopy [12]. Energy-dispersive X-ray spectrometry analysis showed an increase in the calcium-to-phosphorus ratio (Ca/P) in the laser-irradiated enamel covered by biofilm compared with non-irradiated samples [12]. Observations from scanning electron microscopy (SEM) showed that no evidence indicated melting, fusion or other morphological changes in CO_2 laser–treated enamel in comparison with non-treated enamel [11], whereas SEM photomicrographs of laser-irradiated enamel surfaces revealed the typical appearance of melting, cracks and craters with discontinuities in another study [14]. In addition, an increase in surface microhardness was found in laser-treated enamel compared with the negative control [13,14], which demonstrated that CO_2 laser irradiation inhibited the progression of caries-like lesions.

Actions of CO_2 lasers combined with topical fluorides on demineralized enamel and dentin

Eight studies investigated the combined effects of 10, 600-nm CO_2 laser irradiation and the application of topical fluorides on demineralized enamel, whereas the results of these studies varied. Five studies found a synergistic effect between laser irradiation and fluoride application in inhibiting enamel demineralization [16-18,22,23], whereas three other studies found that the combination of laser and fluoride had no additional impact on the inhibition of caries lesion progression in comparison with laser alone [24-26]. Demineralized enamel samples treated with CO_2 laser irradiation in conjunction with the application of amine fluoride showed less calcium dissolution and reduced surface alterations compared with those treated with laser only [16]. Additionally, laser irradiation through topical fluorides significantly enhanced fluoride or calcium fluoride uptake to the enamel surface layer when compared with laser alone [16,26]. Enamel surfaces treated with laser combined with fluoride showed a significantly higher microhardness than that with fluoride or laser only. However, it was also reported that a similar melting appearance was found in enamel surfaces treated with laser associated with or without fluoride [14], and no synergistic effect was found for the inhibition of caries lesion progression [23]. One study investigated the combined effects of 10, 600-nm CO_2 laser irradiation and the application of topical fluorides on demineralized root dentin. The results showed that both main factors had significant effects on the increase of microhardness, but no additive benefit was found by combining these two strategies against the progression of root caries [15].

Discussion

PubMed, Scopus and Web of Science are three of the common research databases for dental research. Thus, they were used in this review for publication retrieval. PubMed is free for the public to access. Most of the journal articles it includes are on the field of medicine and biomedical science and were published after 1950 [27]. PubMed provides multiple versions of literature from early versions before the final versions were published. Scopus belongs to Elsevier, and Web of Science belongs to Clarivate Analytics. They are commercial companies that require access fees to use resources from the two databases. Most fields of science are covered in the two databases. They are complements to each other because both are not inclusive [28]. Scopus includes articles published since 1966. Web of Science is the oldest comprehensive scientific citation indexing database covering publications that can date back to 1900 [27]. With the use of these three common databases, the results of the search were comprehensive. The results of the retrieval provided useful information on the effects of CO_2 lasers on remineralizing dental caries.

This review focused on the CO_2 laser of 10,600 nm in wavelength, which was the first and commonly used CO_2 laser in dentistry. Most commercially available CO_2 laser devices use this wavelength. The CO_2 laser of 10,600 nm has an absorption coefficient in hydroxyapatite that is 10 times lower than that of 9,600 nm [29]. This allows for deeper penetration and higher fluence by a 10,600-nm CO_2 laser to cause the desired thermal effects on caries inhibition compared with CO_2 lasers at other wavelengths [29]. CO_2 lasers with short pulse durations and high peak power are available with the advancement of technology. The new generation of CO_2 laser machines produce less collateral thermal damage. They are more versatile in dental clinical applications [29].

The results of this review showed three effects of CO_2 laser on dental caries. The first one is the inhibition of the growth of biofilm. Dental biofilms consist of bacteria, a matrix of polysaccharides and other organic materials. They strongly adhere to tooth surfaces. Using chemical agents to remove biofilm is ineffective because they generally cannot penetrate deeply into biofilm [21]. The penetration of laser into biofilm makes it a possible alternative for disrupting or removing dental biofilms. Laser irradiation can affect the gene expression in bacteria. The mechanisms involve the direct absorption of laser by DNA or light-mediated photosensitiser with oxygen, causing DNA damage [30]. In addition, the photothermal effect of CO_2 laser can indirectly induce changes in gene expression.

The reduction in bacteria viability by CO_2 lasers was described as dose dependant [21]. Although a laser at low fluence with a short period of irradiation time had no significant effect on the viability of bacteria, the laser changed their gene expression, resulting in the immobilization of *S. mutans* in biofilm [21]. A CO_2 laser at high fluence revealed lethal effects on *S. mutan*s [21]. The low divergence of the wavelength, scattering and backscattering of photons within the spot size area focused the energy and allowed deep penetration into the biofilm [21]. However, such exposure might cause thermal damage to dental hard tissue and pulp. The biofilm could be removed using a laser of high power and high-energy density, but a melted surface and morphological change were observed on the enamel surface in another study [12]. The effects of laser on biofilm varied depending on laser parameters and irradiation methods. The mechanism included the prevention of the initiation of biofilm formation [20], the alteration of gene expression and the immobilization of *S. mutans* in the biofilm [21], killing the bacteria [12,20,21], and morphological change with melting, fusion and cracklines on the enamel surface, which affected bacteria adhesion [12,20].

Zancope first reported that a CO_2 laser caused morphological changes on the enamel surface, such as fusion and melting [20]. Carbonate in the hydroxapatite structure is unstable and is acid soluble [31,32]. CO_2 laser irradiation on demineralized human enamel removed the carbonate [11]. This increased the microhardness without morphological changes on the surface [13]. However, CO_2 laser irradiation could also cause melting and cracking on the enamel surface in the process of removing carbonate [12]. The cracking on enamel was undesirable because it might facilitate caries development along the cracklines [33,34].

The combination of laser irradiation and fluoride therapy has received much attention for the reduction of dental caries progression. The critical pH for the dissolution of enamel dropped in the presence of fluoride in the irradiated surface [35]. From this literature review, the interaction of various fluoride agents with a laser influenced the outcome of the caries inhibition. Although no synergistic effect on caries progression inhibition was found using acidulated phosphate fluoride on enamel in three studies [17,25,26], differences were found on enamel surface characteristics with the continuous and pulse modes of CO_2 lasers. Morphological changes in melting, recrystallization and cracks were observed. No difference was found in enamel calcium loss between fluoride with the continuous mode of a CO_2 laser, the laser alone and fluoride alone [25]. However, the pulse mode of the CO_2 laser after fluoride application improved the suface microhardness of enamel and calcium fluoride uptake, whereas no morphological changes were reported [17,26]. Different concentrations and acidity of sodium fluoride combined with pulsed laser irradiation showed no synergistic effects [18,24]. Enamel with the topical application of sodium fluoride showed higher microhardness when compared with laser irradiation alone [18,24]. Recently reported enamel treated with laser with nano fluro-hydroxyapatitie had higher mircrohardness compared with nano fluro-hydroxyapatitie alone [22].

Conclusion

This review found that a CO_2 laser (10,600 nm) could remineralize dental caries. Current evidence suggests that a CO_2 laser could increase the acid-resistance of caries lesions and inhibit the growth of cariogenic bacteria and enhance fluoride uptake to demineralized mineral tissues.

Figure 1 Flowchart of the literature search

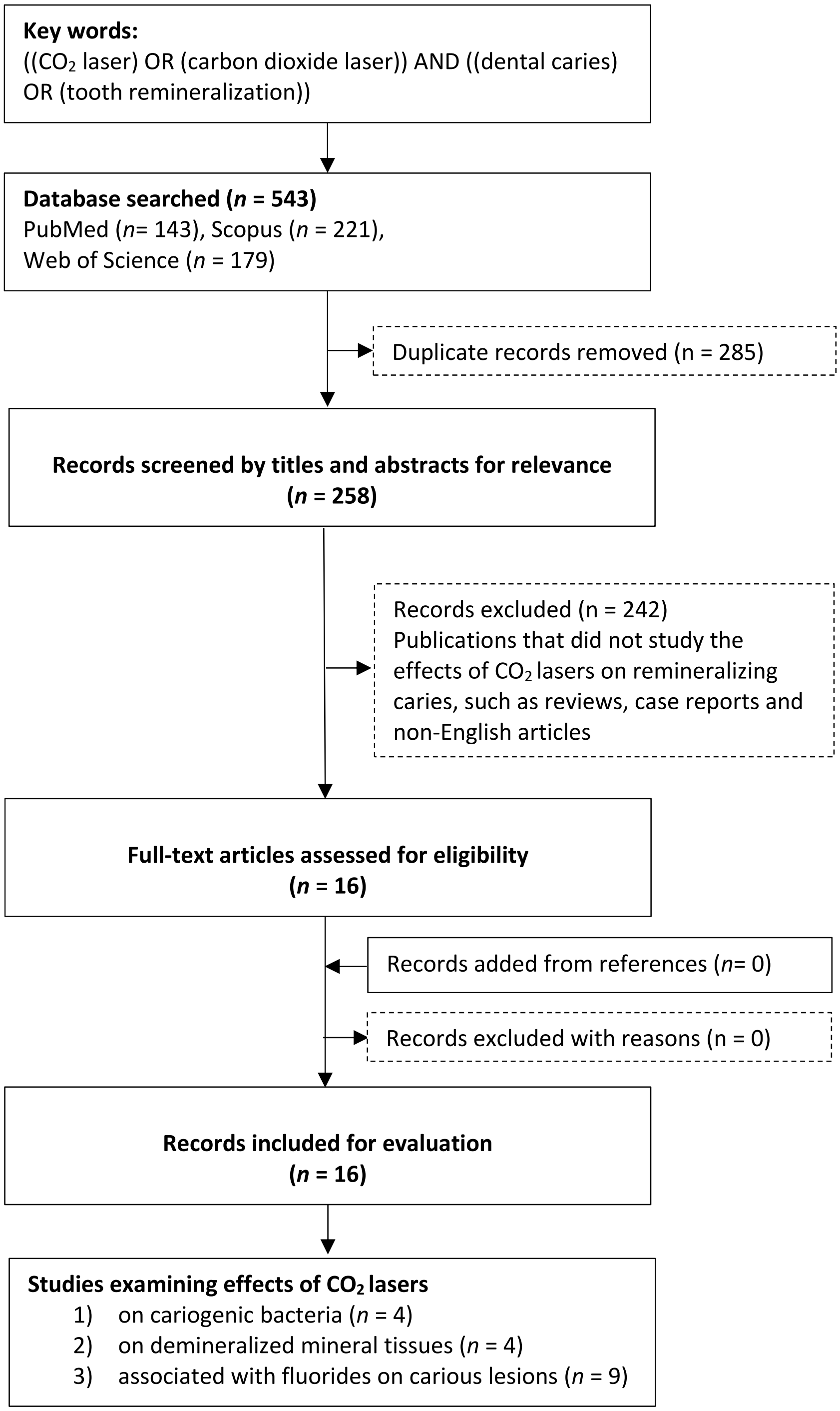

Table 1 Summary of studies of effects of CO_2 (10,600 nm) lasers on cariogenic bacteria

Authors, Year	**Methods**	**Main findings**
Sol *et al*., 2011 [21]	Biofilms of *S. mutans* were irradiated with CO_2 laser before CLSM, SEM and DNA microarray analysis.	A nonsignificant lethal effect was observed at 31 J/cm^2, whereas at higher energy of 70 and 144 J/cm^2, an antibacterial effect was recorded. Laser irradiation at sub-lethal energy downregulated gene expression of *S. mutans*.
Cohen *et al*., 2014 [12]	Bovine enamel cultured with biofilms of *S. mutans* was irradiated with CO_2 laser before SEM and CLSM.	Enamel covered by biofilm showed a smaller melt zone compared with the irradiated without biofilm. A higher proportion of dead bacteria was detected on the irradiated enamel.
Zancope *et al*., 2016 [20]	CO_2 laser–irradiated bovine enamel was cultured with biofilms of *S. mutans* before dry weight, CFU, polysaccharide analysis, PCR, contact angle, FESEM and fluorescence microscopy.	Irradiated group showed a significantly reduced CFU compared with negative control. No difference was found in gene expression. Treated enamel showed increased contact angle compared with negative control.
Yassaei *et al*., 2018 [19]	*S. mutans* suspension with or without photosensitizer was irradiated with CO_2 laser before CFU.	Laser irradiated with photosensitizer group showed a significantly reduced CFU compared with laser-irradiated-alone group and control group.

CFU, colony-forming unit; CLSM, confocal laser scanning microscopy; CO_2, carbon dioxide laser; DNA, deoxyribonucleic acid; FESEM, field emission scanning electron microscope; PCR, polymerase chain reaction; SEM, scanning electron microscopy.

Table 2 Summary of studies of effects of CO_2 (10,600 nm) lasers on demineralized mineral tissues

Authors, Year	**Methods**	**Main findings**
Tagliaferro et al., 2009 [36]	Demineralized human enamel was irradiated with CO_2 laser before Fourier transform Raman spectroscopy and SEM.	Irradiated enamel showed less carbonate content and no melting, fusion or other physical changes compared with the negative control.
Cohen *et al.*, 2014 [12]	Bovine enamel cultured with biofilms of *S. mutans* was irradiated with CO_2 laser before SEM, CLSM, EDS and FTIR.	Irradiated enamel covered with biofilm showed increased Ca/P ratio. Approximately 40% carbonate was lost in the irradiated enamel.
Valerio et al., 2015 [13]	Demineralized human enamel was irradiated with CO_2 laser before MHT.	Irradiated enamel had significantly increased microhardness compared with negative control.
Farhadian et al., 2017 [14]	Demineralized human enamel was irradiated with single or repeated CO_2 laser before FTRS and EDS. They were then subjected to pH cycling for before MHT and SEM.	Irradiated enamel had significantly increased microhardness compared with negative control. Melting and recrystallization of enamel occurred after irradiation.

CO_2, carbon dioxide laser; CLSM, confocal laser scanning microscopy; EDS, energy-dispersive X-ray spectroscopy; FTIR, Fourier transform infrared spectroscopy; FTRS, Fourier transform Raman spectroscopy; MHT, microhardness testing; SEM, scanning electron microscopy.

Table 3 Summary of studies of effects of CO_2 (10,600 nm) lasers combined with fluorides on carious lesions

Authors, Year	Methods	Main findings
Schmidlin *et al*., 2007 [16]	Demineralized human enamel was irradiated with CO_2 laser associated or not with amine fluoride before ion-selective electrode，AAS and SEM.	Irradiated enamel showed increased fluoride uptake. Irradiated enamel combined with fluoride showed less calcium dissolution and reduced surface changes compared with those treated with laser alone.
Steiner-Oliveira *et al*., 2008 [24]	Demineralized human enamel was irradiated with CO_2 laser associated or not with fluorides. They were subjected to pH cycling before PLM and MHT.	The enamel treated with laser and fluoride had no additional effect against caries-like lesion progression compared with those treated with laser alone or fluoride alone.
Chen *et al*., 2009 [25]	Demineralized human enamel was irradiated with CO_2 laser associated or not with APF before an electrolyte analyzer, SEM and PLM. They were then subjected to pH cycling.	The enamel treated with laser and fluoride had no significant differences in calcium loss compared with laser only. Melting, recrystallization and glaze-like surfaces were observed after irradiation.
Colucci *et al*., 2012 [15]	Demineralized human root dentin were irradiated with CO_2 laser associated or not with APF gel before cariogenic challenge and then MHT.	Both irradiated dentin and fluoride treated dentin had increased microhardness. No additive benefit was found by combining laser and fluoride.
Poosti *et al*., 2014 [17]	Demineralized human enamel was irradiated with CO_2 laser associated with APF gel before MHT.	Enamel irradiated with laser combined with fluoride showed a significantly higher microhardness than that with fluoride only.
Souza-Gabriel *et al*., 2015 [18]	Demineralized bovine enamel was irradiated with CO_2 laser associated or not with NaF before MHT.	Irradiated enamel treated with fluoride showed a significantly higher microhardness than that with laser only.
Zancope *et al*., 2016 [26]	Demineralized human enamel was irradiated with CO_2 laser associated or not with APF before SEM and ion-selective electrode. They were subjected to pH cycling before MHT and PLM.	Laser irradiation enhanced "CaF_2"uptake on enamel surface. However, no synergistic effect could be found for the inhibition of caries lesion progression.
El Assal *et al*., 2018 [22]	Demineralized human enamel was covered with pure nHA or nFHA slurries associated or not with CO_2 laser irradiation before MHT and spectrophotometer.	Irradiated enamel treated with nHA or nFHA showed a higher microhardness than those treated with nHA or nFHA alone. Irradiated enamel showed a significantly lower value of color change compared with no laser groups.
Oliveira *et al*., 2018 [23]	Demineralized bovine enamel was irradiated with CO_2 laser associated with various fluoride products before MHT.	Irradiated enamel treated with NaF varnish had significantly higher microhardness compared with those treated with laser alone or laser with other fluoride products.

AAS, atomic absorption spectrometry; APF, acidulated phosphate fluoride; CO_2, carbon dioxide laser; CPP-ACP, casein phosphopeptide-amorphous calcium phosphate; NaF, sodium fluoride; nano hydroxyapatite (nHA); nano fluoro-hydroxyapatite (nFHA); PLM, polarized light microscopy; MHT, microhardness testing; SEM, scanning electron microscopy.

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