Effects of 10,600 nm carbon dioxide lasers on preventing caries

A literature review

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Introduction

Although dentistry has benefitted from technological advancements in recent years, dental caries remains a major oral health problem in most industrialised and non-industrialised countries affecting more than half of schoolchildren and a large majority of adults.[1] Dental caries is a localised chemical dissolution of dental hard tissues caused by the action of acidic by-products of the metabolic processes of cariogenic biofilm.[2] Conventional non-invasive strategies for caries prevention include oral health education, reduction of sugar consumption, use of fluoride, and application of pit and fissure sealants. Fluoride principally works by hindering the process of demineralisation of enamel and dentine and promoting remineralisation of tooth surfaces with early signs of mineral loss. Pit and fissure sealants generate a physical barrier to prevent the access of dental plaque and its acid products from damaging the enamel surface. However, dental sealants are only effective on the pit and fissures and not the smooth surfaces of teeth. New strategies, such as casein phosphopeptide amorphous calcium phosphate[3] and micro- or nanohydroxyapatite compounds, have been proposed to control the balance between demineralisation and remineralisation. It is essential to develop new caries preventive methods to control the disease. A novel, non-invasive approach is the use of laser irradiation on enamel or dentine in preventing caries development. A number of studies reported the potential of laser irradiation on tooth roots or enamel in inhibiting formation of caries lesions.[4–9]

Several types of laser were studied for caries prevention. The wavelengths of neodymium-doped yttrium aluminium garnet (Nd:YAG) lasers (λ = 1,064 nm) and argon lasers (λ = 488–514 nm) make them difficult to be absorbed by enamel. On the other hand, carbon dioxide (CO_2) lasers (λ = 9,000–11,000 nm) are highly absorbed by dental hard tissues and thus have good potential for use in caries prevention.[7,9] The first CO_2 laser adopted a mixture of nitrogen, helium, and CO_2, and CO_2 acted as the active laser medium.[10] Subsequent CO_2 lasers produced various emission laser lines with wavelengths ranging from 9,000 to 11,000 nm. The most common laser lines of CO_2 lasers are centred at 9,300; 9,600; 10,300; and 10,600 nm, respectively. CO_2 laser wavelengths have a higher absorption coefficient to hydroxyapatite than water. A conventional CO_2 laser-emitting light at 10,600 nm is well-absorbed by minerals, while 9,600 nm has the best absorption coefficient to hydroxyapatite followed by 9,300 nm.[1] However, the 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 CO_2 lasers in caries prevention has been studied since the 1960s,[1] when CO_2 lasers (10,600 nm) were discovered to significantly inhibit enamel caries progression.[7] Significantly less demineralisation was also found in CO_2 laser-treated (λ = 10,600 nm) dentine than non-lased dentine.[9] Furthermore, promising effects of combined CO_2 laser irradiation and fluoride treatment in preventing enamel and dentine caries were reported.[11–13] However, the mechanism of caries prevention of CO_2 lasers remains to be elucidated. A literature search using the databases PubMed, Scopus and Web of Science revealed no comprehensive review to evaluate studies investigating the effects of actions of CO_2 lasers in caries prevention. Therefore, the objective of this paper was to systematically review the evidence regarding the effects of CO_2 lasers (λ = 10,600 nm) on preventing dental caries.

Methods

Search strategy

Two investigators (KL and ISZ) performed a systematic search of articles archived in three databases, PubMed, Scopus and Web of Science. The following keywords were used to identify relevant articles: [(CO_2 laser) OR (carbon dioxide laser)] AND [(dental caries) OR (tooth remineralisation)]. There was no publication year limit, and the last search was made on 31 January 2019. Studies published in English through 2018 and archived in the

PubMed, Scopus, and Web of Science databases were chosen. A list of potentially eligible articles was compiled of publications featuring the keywords (Fig. 1).

Study selection and data extraction

Records identified from database searches were checked for duplication. The titles and abstracts from the potentially eligible list were screened after removing duplicate publications. Articles that did not focus on the effects of CO_2 lasers on preventing dental caries were excluded after screening of titles and abstracts. The remaining articles were retrieved with full texts. The reference lists of all the included articles were screened to identify all possibly eligible studies. The inclusion criterion for selecting studies for this review was that studies investigated the effects of CO_2 lasers on preventing enamel and dentine caries, including their combined 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 prevention of caries: reduction of carbonate content, lesion depth, microhardness, mineral loss, surface morphology, and bacterial counts), and the main findings. Any disagreements on study inclusion or data extraction were discussed by the two authors with a third author (OYY) until consensus was reached.

Results

The initial literature search identified 543 potentially relevant articles (143 articles in PubMed, 221 in Scopus, and 179 in Web of Science). A total of 285 duplicate records were removed. After screening the titles and abstracts, 236 articles that were classified as literature reviews, case reports, non-English articles, or irrelevant studies were excluded. No additional relevant publications were found from the references of the selected papers. Finally, 22 articles were found to meet the inclusion criteria and were included in this review. Among these articles, nine studies examined the action of CO_2 lasers on preventing enamel caries (Tab. 1), three studies investigated the effect of CO_2 lasers on preventing dentine caries (Tab. 2), eight studies investigated the effect of CO_2 lasers combined with topical fluorides on enamel (Tab. 3), and three studies examined the effect of CO_2 lasers combined with topical fluorides on dentine (Tab. 4).

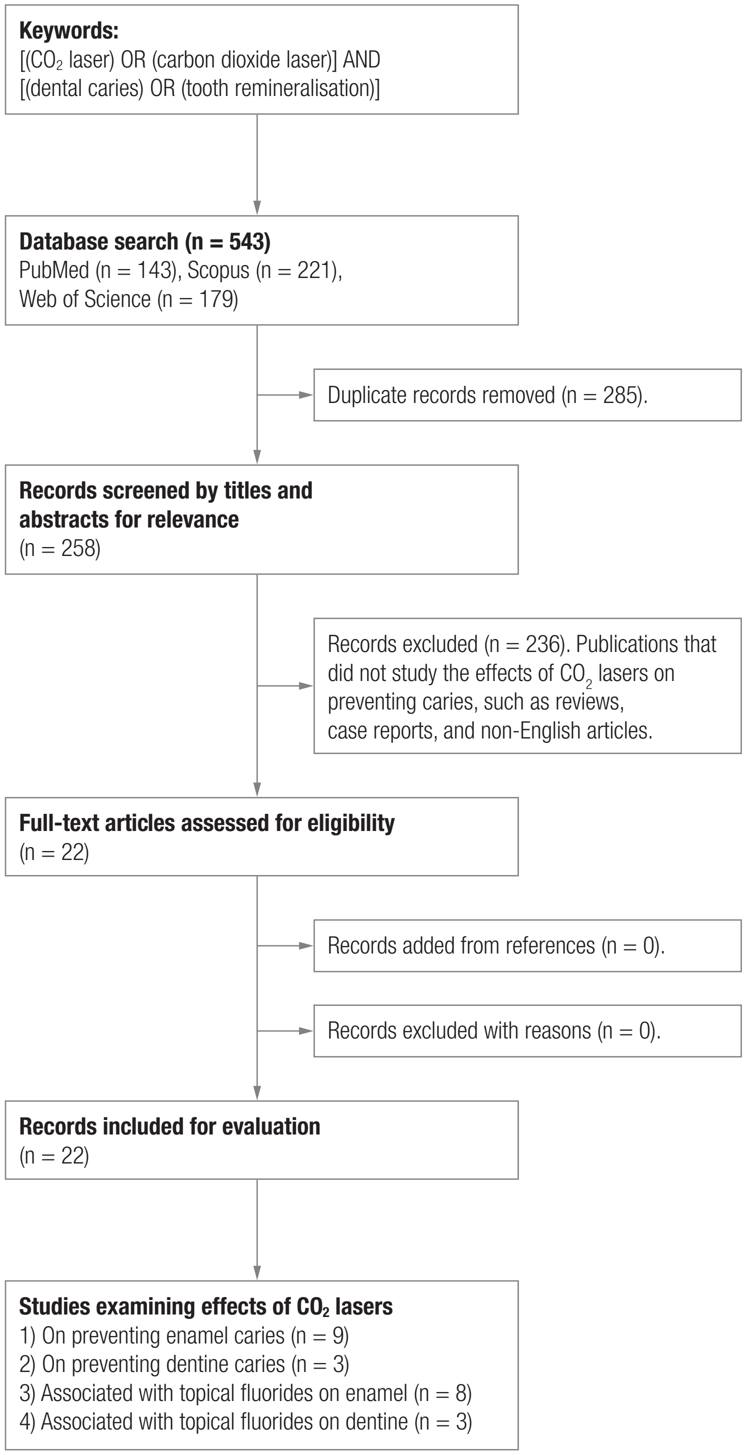

Fig. 1: Flowchart of the literature search.

Effects of CO_2 lasers on preventing caries of enamel and dentine

Nine studies investigated effects of 10,600 nm CO_2 lasers on morphological and chemical changes of enamel as well as on the reduction of enamel demineralisation. Concerning the microhardness analyses, CO_2 laser-treated enamel surfaces showed significantly higher values than those of negative control.[14,15] Polarised light microscopy evaluation revealed that laser-treated enamel groups showed significantly lower lesion depth compared with the non-lased controls,[16,17] and the decreased lesions represented up to 87 % inhibition of the caries progression.[8] The values of mineral loss of enamel calculated from cross-sectional microhardness analyses were statistically lower in laser-irradiated groups than

Authors, year	Methods	Main findings
Vieira et al. 2015[14]	Human enamel was irradiated with CO_2 laser before FTRS and EDX. They were subjected to pH cycling before MHT and SEM.	Irradiated enamel increased microhardness and reduced carbonate content more than negative control. Melting and recrystallisation of enamel occurred after irradiation.
Correa-Afonso et al. 2012[15]	Human enamel irradiated with CO_2 laser was subjected to pH cycling before MHT, PLM, and SEM.	Enamel increased microhardness and reduced demineralisation after irradiation. No fusion, melting, or exposure of enamel prisms was found on the irradiated enamel.
Souza-Gabriel et al. 2010[18]	Human and bovine enamel were irradiated with CO_2 laser before SEM. They were subjected to pH cycling before MHT.	Enamel showed melting and recrystallisation after irradiation. It was more resistant to demineralisation than the negative control.
Esteves-Oliveira et al. 2009[17]	Bovine enamel was irradiated with CO_2 laser before SEM. It was subjected to pH cycling before PLM.	Irradiated enamel showed no ablation, melting, or cracks. It was more resistant to demineralisation than the negative control.
Steiner-Oliveira et al. 2006[20]	Human enamel was irradiated with CO_2 laser before FTRS and SEM. It was subjected to pH cycling before MHT.	Irradiated enamel had less carbonate content and mineral loss than the negative control. Enamel showed melting and fusion after irradiation.
Klein et al. 2005[19]	Human enamel was irradiated with CO_2 laser before SEM. It was subjected to pH cycling before MHT.	Enamel surfaces showed melting and fusion after laser irradiation. They had less demineralisation than the negative control.
Hsu et al. 2000[16]	Human sound enamel with organic matrix removal or not was treated with CO_2 laser and subjected to pH cycling before PLM, microradiography, and SEM.	Irradiated enamel had no surface melting or crater after irradiation. It had less mineral loss and lesion depth than other groups. An interaction effect was found between laser irradiation and enamel organic matrix content.
Featherstone et al. 1998[7]	Human enamel was irradiated with CO_2 laser and then subjected to pH cycling before MHT.	Irradiated enamel showed less mineral loss than the negative control.
Kantorowitz et al. 1998[8]	Human enamel irradiated with CO_2 laser was examined by SEM and subjected to pH cycling before MHT.	Irradiated enamel surfaces showed little or no morphological changes. They had less mineral loss than the negative control.

EDX = energy-dispersive X-ray, FTRS = Fourier-transform Raman spectroscopy, MHT = microhardness testing, PLM = polarised light microscopy, SEM = scanning electron microscopy

Table 1: Summary of studies of effects of CO_2 (10,600 nm) lasers on enamel.

those in non-lased groups.[7,8,16,18–20] There was an interaction effect between the CO_2 laser irradiation and the organic matrix content of enamel on lesion depth and mineral loss of enamel ($p < 0.05$).[16] The enamel with the removal of organic content (non-organic enamel) had a 38 % reduction in lesion depth and a 74 % reduction in mineral loss after laser irradiation when compared to the non-organic enamel without laser irradiation. Both reductions were significantly lower than the results for the lased normal enamel but greater than those for the non-lased enamel.[16] CO_2 laser irradiation could induce chemical changes in enamel. Fourier-transform Raman spectroscopy showed a reduced carbonate content for laser-treated enamel when compared with non-treated ones,[14,20] while there were no statistical differences for calcium and phosphorus components between irradiated groups and the control by energy-dispersive X-ray fluorescence spectrometry measurements.[14]

Observations under scanning electron microscopy revealed evidence of melting and fusion in the enamel samples treated with CO_2 lasers,[14,19,20] and melting and fusion were more frequent in the treated groups that underwent more than one laser application.[14] Enamel surfaces exhibiting melted structures were several times bigger than the prismatic structures and fusion across the prism boundaries.[14] It was verified that a laser-modified layer with a coalescence of crystals was presented in human enamel surfaces, forming an irregular solid mass.[18] A homogeneous and smooth recrystallisation was also observed on the fused enamel surfaces.[14,18] However, some studies found that the treated enamel areas showed little or even no morphological changes.[8,16] The irradiated enamel surfaces exhibited a similar appearance to the non-lased controls,[17] and no signs of surface melting, ablation, crater formation, cracks, or fissures could be observed using the parameters showing caries inhibition effects.[16,17] Three studies investigated the effects of a 10,600 nm CO_2 laser on morphological features of dentine as well as on the reduction of dentine demineralisation.[9,21,22] Root dentine surfaces irradiated with a CO_2 laser with fluences from

Authors, year	Methods	Main findings
de Melo et al. 2014[21]	Human root surfaces irradiated with CO_2 laser were subjected to pH cycling before MHT.	Irradiated root surfaces were more resistant to demineralisation than the negative control.
de Souza-Zaroni et al. 2010[22]	Human root surfaces were irradiated with CO_2 laser before SEM. They were subjected to pH cycling before MHT.	Irradiated root surfaces showed melting and resolidification. They showed less mineral loss than negative control.
Nammour et al. 1992[9]	Human root surfaces irradiated with CO_2 laser were subjected to cariogenic challenge before SEM, microdensitometry measurements, and microradiography.	Root surfaces appeared smooth after irradiation. Root surfaces showed melting with no dentinal openings, and they showed more resistant demineralisation than the negative control.

MHT = microhardness testing, SEM = scanning electron microscopy

Table 2: Summary of studies of effects of CO_2 (10,600 nm) lasers on dentine.

4.0 to 6.0 Jcm^{-2} showed evidence of melting and resolidification under scanning electron microscopy, and a cracking appearance was more evident on those samples treated with 5.0 and 6.0 Jcm^{-2}.[22] Longitudinally fractured samples had a layer of dentine with no tubular structure (20–70 µm thick), whereas the dentinal tubules retained the normal structure below the sealed layer.[9] The values of mineral loss were significantly lower in the laser-irradiated dentine groups than the non-irradiated controls.[21,22] Additionally, laser-induced inhibitory effects on dentine demineralisation were observed when fluences reached or exceeded 4.0 Jcm^{-2}.

Effects of CO_2 lasers combined with topical fluorides on enamel and dentine

Eight studies investigated the combined effects of 10,600 nm CO_2 laser irradiation and the application of topical fluoride on enamel. The results of these studies varied. Four studies found that there was a synergistic effect between laser irradiation and fluoride application in reducing enamel demineralisation,[12,23–25] whereas the other four studies found that the combination of laser and fluoride had no additional impact on decreasing lesion progression when compared with the laser alone.[26–29] Enamel samples treated with laser irradiation in conjunction with the application of titanium tetrafluoride solution showed less calcium loss and increased microhardness than those treated with laser only.[24] Combined sodium fluoride treatment and laser irradiation showed overwhelming effectiveness in preventing enamel demineralisation based on the data analysis of mineral loss and lesion depth.[12] When enamel surfaces were treated with amine fluoride solution immediately followed by laser irradiation, they had markedly reduced cracking and fused and melted areas compared to counterparts treated with the laser alone.[25] Moreover, laser irradiation through the amine fluoride solution significantly increased fluoride uptake to the enamel surface layer compared to fluoride treatment alone.[25] Three studies investigated the combined effects of 10,600 nm CO_2 laser irradiation and application of topical fluorides on dentine, and the results of these studies were consistent, showing a significant synergistic effect of laser irradiation combined with fluoride treatment on the prevention of dentine demineralisation.[11,13,26] The laser combined with fluoride treatment resulted in an 84.5 % decrease in lesion depth,[11] significantly less mineral loss,[26] and lower calcium and phosphorous losses.[13] In addition, the combination of laser and fluoride yielded significantly lower bacterial numbers on dentine surfaces than laser only.

Discussion

The publication search in this review used three databases, PubMed, Scopus, and Web of Science. They are three of the most commonly used and readily available databases. PubMed, which focuses on medicine and biomedical science, provides open access to the public and includes articles published after 1950. One advantage of PubMed is that it provides printed literature as well as early versions before printing publica-

Authors, year	Methods	Main findings
Mahmoudzadeh et al. 2018[29]	Human enamel was irradiated with CO_2 laser associated or not with NaF in different order before SEM. It was subjected to cariogenic biofilm challenge before MHT.	No difference in microhardness was found among enamel treated with laser plus NaF, laser alone, or NaF alone. Irradiated enamel showed melting, cracks, and craters with discontinuities.
Esteves-Oliveira et al. 2017[26]	Bovine enamel was irradiated with CO_2 laser associated or not with NaF. It was subjected to cariogenic biofilm challenge before TMR, CFU, and SEM.	No difference in mineral loss was found between irradiated enamel treated with or without fluoride. The bacterial numbers on enamel were not affected by laser or fluoride.
Mirhashemi et al. 2016[24]	Bovine enamel irradiated with CO_2 laser was treated with TiF4 and subjected to pH cycling before AAS and MHT.	Irradiated enamel treated with TiF4 was more resistant to demineralisation and had an increased microhardness compared to those without TiF4 treatment.
Seino et al. 2015[27]	Human enamel was irradiated with CO_2 laser associated or not with APF before SEM. It was subjected to pH cycling before QLF.	Enamel surface showed no melting after laser irradiation. Irradiated enamel treated with fluoride showed similar resistance to demineralisation compared to those treated with laser only.
Tagliaferro et al. 2007[28]	Human enamel was irradiated with CO_2 laser associated or not with APF. It was subjected to pH cycling before MHT.	Irradiated enamel treated with fluoride showed similar resistance to demineralisation compared to those treated with laser alone.
Tepper et al. 2004[25]	Human enamel was irradiated with CO_2 laser associated or not with amine fluoride before SEM. It was subjected to acid challenge before AAS.	Irradiated enamel had higher fluoride uptake. Irradiated enamel treated with fluoride had less morphological change and similar demineralisation compared to those treated with laser alone.
Hsu et al. 2001[12]	Human enamel treated with sodium fluoride was irradiated with CO_2 laser before pH cycling. It was studied by microradiography and SEM.	Irradiated enamel treated with NaF was more resistant to demineralisation than the control group. Irradiated enamel showed no evidence of surface melting.
Hsu et al. 1998[23]	Enamel irradiated with CO_2 laser associated or not with fluoride was exposed to a demineralising solution before light microscopy and microradiography.	The irradiated and non-irradiated enamel was more resistant to demineralisation in the presence of fluoride. There was a synergism between laser irradiation and fluoride in reduction of enamel solubility.

AAS = atomic absorption spectrometry, APF = acidulated phosphate fluoride, CFU = colony-forming unit, MHT = microhardness testing, NaF = sodium fluoride, QLF = quantitative light-induced fluorescence, SEM = scanning electron microscopy, TiF4 = titanium tetrafluoride, TMR = transverse microradiography

Table 3: Summary of studies of CO_2 (10,600 nm) lasers with fluoride on preventing enamel demineralisation.

Authors, year	Methods	Main findings
Esteves-Oliveira et al. 2017[26]	Bovine dentine irradiated with CO_2 laser was treated with NaF and subjected to cariogenic biofilm challenge before TMR, CFU, and SEM.	Irradiated dentine treated with NaF was more resistant to demineralisation and yielded lower CFUs than those without NaF treatment.
Esteves-Oliveira et al. 2011[13]	Bovine dentine was irradiated with CO_2 laser associated or not with APF and then subjected to pH cycling before ICP-OES.	Irradiated dentine treated with fluoride had lower calcium and phosphorus concentration in the demineralisation solution than those without fluoride treatment.
Gao et al. 2006[11]	Human root dentine was irradiated with CO_2 laser associated or not with NaF. They were subjected to pH cycling before PLM. Fluoride uptake was characterised by the ToF-SIMS analysis.	Irradiated dentine treated with NaF was more resistant to demineralisation than the control group. Irradiated dentine had a significantly higher fluoride uptake than non-irradiated groups.

APF = acidulated phosphate fluoride, CFU = colony-forming unit, ICP-OES = inductively coupled plasma optical emission spectrometer, NaF = sodium fluoride, PLM = polarized light microscopy, SEM = scanning electron microscopy, TMR = transverse microradiography, ToF-SIMS = time-of-flight secondary ion mass spectrometry

Table 4: Summary of studies of CO_2 (10,600 nm) lasers with fluoride on preventing dentine demineralisation.

tion. Scopus and Web of Science belong to commercial companies, and subscription fees are required to use these two databases, which cover most scientific fields. Scopus includes a wider range of journals than PubMed and Web of Science,[30] and it includes articles published since 1966. Web of Science is the first comprehensive scientific citation indexing database covering the oldest publications. The earliest records date back to 1900.[30] The articles in Web of Science are published in journals with an impact factor. With the use of these three commonly used databases, the results of the retrieval were exhaustive, and they provided comprehensive information on the effects of CO_2 lasers on caries prevention in previous publications. This literature review only included 10,600 nm CO_2 wavelengths, while studies with 9,300 and 9,600 nm wavelengths were excluded. The 10,600 nm wavelength was selected because it has been extensively studied and marketed in the dental field.[31] Moreover, the absorption coefficient of 10,600 nm of enamel and dentine is lower than that of 9,300 and 9,600 nm wavelengths. This allows lasers of 10,600 nm wavelength to be six times and ten times deeper in penetration depth in dental hard tissue than those of 9,300 and 9,600 nm, respectively. Further, 10,600 nm might be the preferred wavelength for caries prevention studies because of its optical property.[24,26]

Enamel and dentine surface irradiated by CO_2 laser either showed little to no surface morphological change[7,8,15–17] or melting, fusion, and recrystallisation.[14,18–20,22] Regardless of surface change, irradiated surfaces showed reductions in carbonate content and increases in microhardness and demineralisation resistance. Surface changes were thought to be related to demineralisation inhibition.[14] Sealing of enamel surface was also suggested to reduce the permeability of enamel surfaces during ion exchange.[32,33] Studies showed that fluence between 5 and 16 Jcm^{-2} produced melting, fusion, resolidification, and recrystallisation on enamel surface.[14,18–20] Lower fluence is required on dentine than on enamel, as higher surface temperature is achieved due to the lower reflectance loss and lower thermal diffusivity of dentine.[21] Morphological variations on melted surfaces, such as droplets, holes,[14] and smooth recrystallined surfaces,[18] might foster resistance to demineralisation. However, undesirable cracks were also observed.[8,22,24] Although surface melting and fusion reduced permeability, surface morphological change was not necessary for enhancing resistance of enamel to demineralisation.[8,15–17] The effect of temperature rise induced by laser in an organic matrix was suggested by Sato.[34] He suggested that the melting and swelling of the organic matrix under heat (300 to 400 °C) blocked the diffusion pathway of calcium, which resulted in calcium loss reduction. Hsu suggested that there may be partial blockage of inter- and intraprismatic spaces.[16] This affected the ion diffusion in enamel and restricted enamel demineralisation. Dentine contains organic and inorganic components similar to enamel, but it is higher in water and organic content by volume. A laser-induced thermal effect at 600 to 900 °C was suggested as a mechanism to reduce or eliminate carbonate content and increase crystallinity to reduce tooth solubility.[21,22]

Calcium fluoride crystals were present on fluoridated surfaces after topical fluoride application.[35,36] The concentration of fluoride on enamel surfaces was shown to increase with application of acidic fluoride agents.[37] Fluoride agents from neutral to strong acidity (low pH value) were studied in this review.[12] Enamel treated with 4 % titanium tetrafluoride (pH 1.2) alone had better resistance to demineralisation than those treated with laser and titanium tetrafluoride.[24] Laser irradiation before or after fluoride application of 1.23 % acidulated fluoride phosphate and 1.23 and 5 % sodium fluoride (NaF) at pH between 3.5 and 4.5 improved demineralisation resistance and microhardness similar to fluoride alone or laser alone.[26–28] There was a synergistic effect in mineral loss reduction using a laser with 2 % NaF neutral solution.[12] It was suggested that laser irradiation in the presence of fluoride resulted in fluorapatite formation as organic matrix was removed.[12] Concentrations of NaF did not seem to be a factor in synergism with lasers.[12,26,28] It might be deducted from the above-mentioned studies that acidic fluoride affected the synergism of laser and fluoride, but it appears that neutral fluoride is related to synergism. Amine fluoride has been demonstrated to superior to sodium fluoride.[38] The amino group binds readily onto enamel enabling fast, even distribution of fluoride over the surface. It was reported that there was a synergistic effect in fluoride uptake and a reduction in enamel solubility using 1 % amine fluoride solution (pH not reported), but there was no significant difference in acid resistance between fluoride alone and laser with a fluoride group.[25] However, the same article concluded that laser with fluoride showed beneficial effect in acid resistance. Synergistic effects of laser and fluoride on dentine did not seem to depend on the sequence of laser and fluoride application.[11,13,26] The use of acidulated phosphate fluoride (pH 3.5 and 1.25 % fluoride) and NaF (pH 4.5 and 2.26 % fluoride) on dentine gave synergistic effect in reduction in calcium loss and mineral loss.[13,26] However, laser with the same fluoride concentration and acidity did not show synergistic effect on enamel. The use of 2 % neutral NaF solution with laser showed synergistic effect on dentine as well as enamel, as discussed earlier. The combination of NaF and laser irradiation resulted in significantly higher uptake of fluoride and lesion depth reduction than fluoride or laser alone.[11] Fluoride interacts with teeth by incorporating into hydroxyapatite crystals. The formation of calcium fluoride-like material on the surface was thought to be the main factor in caries reduction.

There were a few postulated mechanisms of combined laser and fluoride. Laser-induced temperature increase resulted in loss of carbonate in the crystalline structure, which was substituted by fluoride ions, enhancing fluoride uptake.[11] The use of laser to modify dentine surface energy might cause more stable absorption of calcium fluoride.[13,26] The fluoride ions released by calcium fluoride could reduce demineralisation and enhance remineralisation. The main reason for reduction in lesion depth might be the result of fluoride that firmly bound to root surfaces, acting as a fluoride reservoir against demineralisation.[11] Therefore, the effect of CO_2 laser irradiation on the lesion depth of dentine needs further investigation. The combined effect of laser and fluoride was also likely to be related to effect on enamel and dentine surfaces. Synergistic effects were achieved with different sets of laser parameters on enamel and dentine with 2 % neutral NaF solution.[11,12] There were many variables in laser parameters that could influence the temperature increase and changes on enamel and dentine surfaces.[13] Parameters such as pulse durations, energy densities, irradiation methods, and total pulses irradiated per spot area are not discussed in this review.

Conclusion

In this review, studies found that CO_2 (10,600 nm) lasers could prevent demineralisation of enamel and dentine. Although the exact mechanism is not well-elucidated, current evidence suggests that CO_2 lasers have a synergistic effect with fluoride in preventing the demineralisation of dentine.

Compliance with ethical standards: the authors declare that they have no conflict of interest.

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Literature

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