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Laser induced enamel remineralization: A systematic review

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Abstract
Background: This systematic review aimed to investigate the efficiency of Laser induced enamel remineralization.
Review Method: An extensive electronic search for *in vitro* Randomized control trials and Clinical control trials via Medline (via PubMed), The Cochrane Controlled Clinical Trials Register databases up to date 3/11/2018 was done. Articles were retrieved and exported to Mendeley Desktop 1.13.3 software.
Results: In total, 18 articles were selected for review out of 102 articles retrieved from the search and remaining were excluded based on the eligibility criteria. Majority of articles (more than 90%) pointed out towards better laser induced remineralization effect compared to control group (fluoride therapy and other non-fluoride remineralizing agents) Laser therapy using Low level and Hard tissue lasers (CO_2, Er: YAG, Er, Cr: YSGG, Nd: YAG and diodes) demonstrated efficient enamel remineralization *in vitro*.
Conclusion: Used in conjunction with or as a replacement for conventional enamel remineralization methods, Laser induced enamel remineralization seems to have a promising future.

Keywords: Enamel carious lesion, remineralization, low level laser, hard tissue laser

1. Introduction

Dental caries is one of the most common preventable childhood disease and people are susceptible to the disease throughout their lifetime. It is the primary cause of oral pain and tooth loss. Though it can be arrested and potentially reversed in its early stages, it is often not self-limiting and without proper care, caries can progress until the tooth is destroyed [1]. It is a multifactorial disease that starts with microbiological shifts within the complex biofilm and is affected by salivary flow and composition, exposure to fluoride, consumption of dietary sugars, and by preventive behaviours (cleaning teeth). Dental caries pathophysiology is not simply a continual cumulative loss of tooth minerals, but rather a dynamic process characterized by alternating periods of demineralization and remineralization. Lesion progression or reversal depends on the equilibrium between demineralization-favouring pathological factors (cariogenic bacteria, fermentable carbohydrates, salivary dysfunction) and the protective factors (antibacterial agents, sufficient saliva, remineralizing ions) that tip the balance towards remineralization [2]. Remineralization can occur as a natural repair process where plaque/salivary calcium (Ca2+) and phosphate (PO4 3–) ions are deposited into crystal voids of the demineralized tooth structure, resulting in net mineral gain. The presence of free fluoride (F–) ions in the oral environment can drive the incorporation of Ca2+ and PO4 3– ions into the crystal lattice, with the ensuing fluorapatite mineral significantly more resistant to a subsequent acid challenge [3].

A better understanding of regenerative and physiochemical mechanisms has influenced the development of a number of innovative remineralization technologies that go beyond fluoride-mediated remineralization. While traditional fluoride-based remineralization remains the cornerstone for caries management with the highest level of supporting evidence, additional remineralizing agents to enhance fluoride effects are often needed in high caries risk individuals and population groups. Laser irradiation has been used in recent years for its remineralizing effect on tooth structure. It has been indicated that high power lasers such as CO_2 laser can increase enamel surface hardness and reduce its solubility. For caries prevention, in order to alter the composition or solubility of dental hard tissues, the laser light must be strongly absorbed and converted efficiently to heat without damage to underlying or surrounding tissues [4].

Therefore, specific wavelengths must be chosen where absorption is high in regions which correspond to specific components in dental hard tissues, such as hydroxyapatite and water which are the main targets of enamel remineralization. Many laser systems like CO_2, Er:YAG, Er,Cr:YSGG, Nd:YAG and diodes have shown promising results in enamel remineralization [4]. This systematic review investigated the efficiency of Laser induced enamel remineralization using different energies and wavelengths of lasers through invitro randomized controlled trials.

2. Method

2.1 Literature retrieval

An extensive electronic search was made on 3 databases namely Medline (via PubMed), The Cochrane Controlled Clinical Trials Register and Scopus up to date 3/11/2018. Hand searching was performed in the relevant journals. Terms used in the search included "Sub ablative laser in remineralization", "Low level laser therapy in enamel remineralization/demineralization", "diode lasers in enamel remineralization/demineralization", "Er: YAG laser and caries", "Er: YAG laser and enamel demineralization/ remineralization", "Er: YAG laser and caries prevention". Reference lists of the retrieved were also checked. No restrictions on the language or date of publication was applied during the search.

2.2 Criteria for article selection

Articles were retrieved based on PICOS criteria: (Table 1)

Table 1: PICOS format (Population, Intervention, Control, Study design) protocol formulated to identify studies pertaining to research question formulated.

Population	Early enamel carious lesions induced on deciduous or permanent teeth specimens
Intervention	Laser induced remineralization with Hard tissue and diode laser of any wavelength
Control	Fluoride or non -fluoride induced enamel remineralization and/ or no treatment
Study design	*In vitro*, Randomized controlled/ clinical controlled trials

Inclusion criteria

1. Laser of any wavelength in pulsed or continuous wave mode applied for remineralization/prevent demineralization
2. Only invitro, Randomized Clinical Trials, Clinical control trials, on extracted human teeth specimens
3. Outcome based on calcium loss on demineralization, Surface hardness, Scanning electron microscopic findings
4. Laser application compared along with various forms of fluoride and non-fluoride remineralizing agents applied to permanent or primary dentition in an *in vitro* study design.

Exclusion criteria

1. Any other study design such as case reports, review articles, letters, descriptive studies etc.
2. Animal trials
3. Studies in which application of laser has been done for other purpose such as bleaching or sensitivity, erosion etc.
4. Each study was reviewed by two authors independently and any difference of opinion was resolved by reaching a consensus and if necessary, resolved by a third reviewer. The review authors were not blinded to authors, institution or journal. All full text papers that were retrieved were similarly screened.

2.3 Data extraction and quality appraisal

Data and quality information was extracted and fed into Revmann 5.3 software. The Year of publication and country of origin was recorded. Inclusion/Exclusion criteria were specified and a detailed description of interventions was given. All outcomes as reported in trials were tabulated.

3. Results

The search strategy yielded a total of 102 articles. (Table 2) Post removal of duplicates, articles were retrieved, and their materials and methods were scanned and reviewed for PICOS criteria and eligibility criteria. This yielded a total of 18 articles which were systematically reviewed.

Table 2: Articles retrieved from various databases

Database	Search strategy	Articles retrieved
PubMed	("dental enamel"[MeSH Terms] OR ("dental"[All Fields] AND "enamel"[All Fields]) OR "dental enamel"[All Fields] OR "enamel"[All Fields]) AND remineralization[All Fields] AND demineralization[All Fields] AND ("lasers"[MeSH Terms] OR "lasers"[All Fields] OR "laser"[All Fields])	81
Cochrane Database of Clinical trials	Laser AND Denral enamel AND Remineralization. Er:YAG AND Enamel demineralization	8
Scopus	"Sub ablative laser in remineralization", "Low level laser therapy in enamel remineralization/demineralization", "diode lasers in enamel remineralization/demineralization", "Er:YAG laser and caries", "Er:YAG laser and enamel demineralization/remineralization", "Er:YAG laser and caries prevention".	13

3.1 Characteristics of the studies: Studies included in systematic review were reported in India, Iran, Brazil and Taiwan. All the studies followed *in vitro* trial on human extracted teeth. Studies reported intervention on deciduous canines, incisors and molars and permanent premolars of maxillary and mandibular arches. Laser therapy was performed using GaAlAs diode laser [5, 6, 7], CO_2 laser [8, 9, 10, 11], Er,Cr:YSGG [12, 13], Nd:YAG laser [14, 15], Infrared laser [16] and Er:YAG [7, 17, 18] at various laser parameters like power density, power output, wavelength, time, frequency, mode of application and dose. The test group was considered as only Laser therapy in the present review which was compared with various groups like control group (no treatment), fluoride treatment groups like APF gel [11, 13] and Sodium fluoride varnish, CPP-ACP creme group (MI paste) [6, 7], Remin Pro group [5] and laser therapy prior or after fluoride therapy or CPP-ACP therapy [19, 20, 21, 22]. (Table 3)

Table 3: Characteristics and laser parameters used in studies

	Author; Year; place	Specimens	Sample size per group	Laser group parameters	Comparison Group	Result
1	Ahrari *et al.* 2011; Iran	premolars	12	(GaAlAs) diode laser 810 nm; continuous-wave mode, 90 seconds. - 500 mW	Control, NaF, MI Paste plus, Remin Pro®, NaF + Laser, MI Paste Plus + Laser, Remin Pro® + Laser.	Control, Laser and Remin Pro® groups did not show significant remineralization effect.
2	Kamverdi *et al.* 2018; Iran	Premolars	15	CO_2 laser (λ = 10.6 μm), 0.5 W power 0.44 J/cm^2 energy density.	Control group, CPP-ACP and laser combined CPP-ACP treatment.	CO2 laser +CPP-ACP showed highest remineralization effect
3	Kumar P *et al* 2016. India	Premolars	20	Er,Cr:YSGG laser irradiation 0.5 Watt; 10 seconds; 20 Hz; Air =40 % and Water = 60%. 5.55 W/cm^2 with fluence: 0.28 J/cm^2.	Control (No treatment), Er,Cr:YSGG laser irradiation followed by 2% NaF gel, laser irradiation and 1.23% APF gel, 2% NaF gel pretreatment followed by laser irradiation.	2% NaF gel pretreatment followed by Er, Cr:YSGG laser irradiation showed maximum remineralization effect
4	Hemmati *et al.* 2016; Iran	Deciduous incisors	12	CO2 laser; diode laser (810nm); 11.3 or 20.0 J/cm^2, 0.4 or 0.5 W	NaF varnish (2.26% F); NaF varnish + diode laser; NaF varnish + CO_2 laser; control group (no treatment).	The NaF + diode laser group had significantly higher remineralization effect than the other groups
5	Zancope *et al.* 2016; Brazil	Primary teeth	15	Carbon dioxide (CO_2) (λ 10.6 µm) laser irradiation (11.3 or 20.0 J/cm^2, 0.4 or 0.7 W	Carbon dioxide (CO_2) combined with APF gel application	CO_2 laser irradiation, combined with a single APF showed highest remineralization effect
6	Rocha *et al.* 2016; Brazil	Primary molars	13	CO_2 laser pulse mode; 100 µs pulse duration, 4-mm working distance, for 10 s,0.5, 1.0 or 1.5 W	(control) ;0.4 % stannous fluoride gel (SnF_2)	Laser therapy alone showed maximum remineralization effect
7	Velerio *et al.* 2015; Brazil	Primary Canines	10	CO_2 laser (λ = 10.6 μm), 0.5 W power 0.44 J/cm^2 energy density.	APF: 1.23%, treatment (control).	CO_2 laser group showed highest remineralization effect
8	Bahrololoomi *et al.* 2015; Iran	Primary molars	30	Diode laser at 5 W power, 980nm, 5 sec, contact mode and, diode laser at 7 W power.	5% NaF varnish ; NaF varnish+ diode laser	There was no significant difference in remineralization effect between groups.
9	Asl-Aminabadi *et al.* 2015; Iran	Premolars		Nd:YAG laser, 1.064 µm non-contact mode, quartz fiber diameter 200 µm for 15 s: 100 mJ, 125 J/cm^2, 10 Hz 1 W	Distilled water, CPP-ACP crème, CPP-ACP plus laser.	CPP-ACP plus laser therapy showed highest remineralization effect.
10	Heravi *et al.* 2014; Iran	Premolars	10	CPP-ACPF cream + red laser (660 n m), CPP-ACPF cream +810 nm, Er:YAG +CPP-ACPF.	CPP-ACPF cream, control (no treatment)	CPP-ACPF cream + red laser (660 n m) and Er:YAG +CPP-ACPF produced higher remineralization effect
11	Yassaei S *et al.* 2014; Iran	Permanent premolars	15	Er:YAG laser emitting at a wavelength of 2.94-mm, 80 mJ of energy, 4 Hz frequency for 10 s and energy per pulse of 80 mJ with water spray and 1.2 mm spot size in non-contact mode	control, MI Paste Plus, Laser and MI	Laser and Laser combined with MI paste showed more remineralization effect
12	Poosti *et al.* 2013; Iran	Premolars		APF +CO_2 laser applied (10 mJ, 200 Hz, 10 s)	Control, APF	Co2 applied before APF treatment showed highest remineralization effect
13	Gabriel *et al.* 2010; Brazil	Primary teeth	12	CO_2 laser 10.6 μm), 0.5 W power 0.44 J/cm^2 energy density.	5% sodium fluoride varnish, 1.23% acidulated phosphate fluoride (APF) gel, or no treatment (control).	Remineralization effect was highest in laser group followed by varnish group and APF group
14	Chen *et al.* 2009; Taiwan	Permanent canines	20	Nd:YAG laser only	control group, APF only, APF+ Nd:YAG laser group, APF+CO(2) laser group, Nd:YAG laser+ APF group,	Laser along with fluoride therapy improved the enamel remineralization effect
15	Moslemi *et al.* 2009; Iran	premolars	17	Er,Cr:YSGG laser; laser-irradiated followed by APF treatment; and APF-treated followed by laser irradiation.	untreated control group, 1.23% APF gel	Er,Cr:YSGG laser along with APF gel showed maximum remileralization effect
16	de Sant'Anna *et al.* 2009; Brazil	Primary molars	4	infrared laser treatment (L) (λ = 810 nm, 100 mW/cm^2, 90 sec, 4.47 J/cm^2, 9 J);	CTR-no treatment; infrared laser irradiation and photo-absorbing agent (CL); photo-absorbing agent alone; infrared laser irradiation and fluoridated photo-absorbing agent (FCL); and	infrared laser irradiation with photo-absorbing agent showed maximum remineralization effect

					fluoridated photo-absorbing agent alone (FC).	
17	De Frietas *et al*. 2008; Brazil	Third molars	9	Er,Cr:YSGG laser at 0.25 W, 20 Hz, 2.8 J/cm^2; Er,Cr:YSGG laser at 0.50 W, 20 Hz, 5.7 J/cm^2; Er,Cr:YSGG laser at 0.75 W, 20 Hz, 8.5 J/cm^2;	G4—sodium fluoride (NaF) dentifrice (positive control); G5—no treatment (negative control).	Er,Cr:YSGG laser irradiation at 8.5 J/cm^2 showed highest remineralization
18	Castellan *et al*. 2007; Brazil	Deciduous molars	10	Er:YAG laser (2 Hz, 60 mJ, 40.3 J/cm(2)); G4, Nd:YAG laser (80 mJ, 10 Hz, 0.8 W).	negative control and fluoride	Laser groups caused more remineralization than control group

3.2 Review of studies
Majority of studies 16 out of 18 studies showed beneficial effects of laser therapy alone and laser therapy along with other fluoride and non-fluoride remineralizing agents in remineralizing artificially induced early enamel carious lesions on extracted human teeth *in vitro*. However, two studies by Ahrari *et al*., [5] and Bahrololoomi *et al*., [8] showed no significant differences between laser and control group. These studies tried Diode lasers at 810nm and 980 nm respectively unlike other studies which showed significant differences in remineralization effects where CO_2 laser, Er,Cr:YSGG, Nd:YAG laser, Infrared laser and Er:YAG lasers were used [8-15]. Laser therapy along with topical fluorides showed more beneficial effect compared to laser alone [6, 7, 11, 13]. Pre-treatment with topical fluoride before laser therapy showed higher remineralization effect in a study where Er;Cr:YSGG was used [12]. However with CO_2 laser therapy post treatment with topical fluoride showed higher remineralization potential [11]. Laser therapy along with non - fluoride remineralizing agents like CPP-ACP showed higher remineralizing effects [7, 14]. Application of photo absorbing agent to teeth before laser therapy improved remineralization effects in a study done by de Sant'Anna *et al*.[16]

4. Discussion
Shafer defined dental caries as, an irreversible microbial disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substance of the tooth, which often leads to cavitation [23]. It is a complex and dynamic process where a multitude of factors influence and initiate the progression of disease. Demineralization and remineralization are balanced processes that normally occur in the oral cavity. Sometimes, diet variations, oral hygiene or microbial activity can lead to the predominance of demineralization. Remineralization is facilitated by the buffering action of saliva, permitting calcium and phosphate ions to precipitate onto the tooth and form new mineral [23]. Therefore, modulation of the demineralization-remineralization balance is the key to prevention of dental caries. Until recently, the conventional treatment concept for all carious teeth involved caries excavation and replacement with a restorative material. However, with decades of research, evolved the “minimally invasive” approach which incorporates detecting and treating these areas sooner, emphasizing on prevention, rather than the traditional surgical model.
Fluoride has been gold standard therapy for its cariostatic potential. Despite its profound effect in halting caries progression, it does not aid in eliminating caries totally. Increased fluoride concentration can produce detrimental effects on the tooth.Furthermore, the availability of calcium and phosphate ions can be a limiting factor for fluoride retention and for net remineralization to occur. This requirement has refocused the research to develop preventive agents functioning as an adjunct/independent to fluoride. Many non-fluoride remineralizing agents like CPP-ACP(Casein phosphopeptide Amorphous calcium phosphate), Xylitol, Dicalcium phosphate dihydrate, Amorphous calcium phosphate, Bioactive Glass Materials, Nano hydroxyapatite, Arginine bicarbonate calcium carbonate complex, Tricalcium phosphate, Trimetacalcium phosphate etc. have been tried [24].
Laser induced enamel remineralization has emerged as a novel and promising therapy for caries prevention. It has been demonstrated that the application of a high-power lasers, such as CO2 [8, 9, 10] and erbium lasers (erbium:yttrium-aluminium-garnet (Er:YAG) [7, 17] and erbium, chromium:yattrium-scandium-gallium-garnet (Er, Cr:YSGG) [12, 13], are effective in white spot lesion prevention. These lasers absorb water from the hydroxyapatite of tooth tissues and can modify the crystalline structure, acid solubility, and permeability of the tooth surface to increase resistance against enamel demineralization [4]. Suggested mechanisms of acid resistance include; Lased surfaces with crater-like holes 1-20 μm in diameter showing positive birefringence and reversal of birefringence after acid challenge of the lased enamel also there was improvement in crystalinity after Er:YAG ablation in addition to this there was different mechanical surface alterations such as reduced enamel solubility without severe enamel alteration [4]. However few studies demonstrated undesirable effects causing fine enamel cracks, which were starting points for acid attack, causing deep demineralization and respectively a reduction of positive effect of enamel caries prevention [25]. Also, high-power lasers are costly and not readily available in every practice. High-energy laser treatment has been used to melt the enamel and to ‘seal’ the surface for caries prevention. However, clinicians are concerned that high powered lasers may potentially damage the gingival or pulpal tissues [26].
To overcome the short comings of high energy lasers Low Level Lasers (Diodes with 660nm-980nm wavelengths) were considered for enamel remineralization. Low level lasers are relatively inexpensive, small, and portable and have multiple applications in several areas of dentistry. Equally, their application in the prevention or arrestment of tooth caries is interesting [16]. A study employing low-energy laser treatment achieved more than 90% reduction in enamel demineralization, which indicated that melting enamel may not be necessary for laser-induced caries prevention (LICP), and the inhibition of enamel diffusion through the modification of organic matrix (OM) may be one of the major mechanisms involved in LICP [5]. This unconventional mechanism to block enamel diffusion was associated with ‘organic blocking’ induced by lower-energy laser treatment, which preserves and modifies the organic matrix to obliterate the diffusion channels in enamel, in contrast to ‘inorganic blocking’ caused by high-energy laser therapies, which melts enamel hydroxyapatite [5]. Laser-tissue interactions are mainly controlled by laser parameters such as wavelength, energy density, pulse duration, exposure time, emission mode, and repetition rate. Among these parameters, pulse duration and

energy density were found to influence the ablation threshold significantly [27]. Numerous studies have been carried out wherein authors have used commercially available remineralizing agents along with laser to improve the remineralizing efficacy which has been proven to be effective rather than using commercially available products alone. More research needs to be carried out adopting meta-analysis and in- vivo research designs which can resolve the research equipoise in this field.Used with or as an adjuvant therapy for conventional remineralizing agents, it is expected that specific laser technologies will become an essential component of contemporary dental practice over the next decade.

5. Conclusion

Majority of studies reviewed showed beneficial effects of laser therapy alone and laser therapy used as adjuvant along with fluoride and non- fluoride remineralizing agents in remineralizing artificially induced early enamel carious lesions on extracted human teeth *in vitro*. CO_2 laser, Er, Cr:YSGG, Nd:YAG laser, Infrared laser, Er:YAG lasers and Low level Diode lasers were used. Laser therapy along with topical fluorides showed more beneficial effect compared to laser alone. Application of photo absorbing agent to teeth before laser therapy improved remineralization effects. Laser induced enamel remineralization seems to have a promising future.

6. References

1. Pitts NB. Are we ready to move from operative to non-operative/preventive treatment of dental caries in clinical practice? Caries Res. 2004; 38:294-304.
2. Konig KG. Clinical manifestations and treatment of caries from 1953 to global changes in the 20th century. Caries Res. 2004; 38:168-72.
3. Marthaler TM. Changes in dental caries 1953–2003. Caries Res. 2004; 38:173-81.
4. Karandish M. The efficiency of laser application on the enamel surface: a systematic review. Journal of lasers in medical sciences. 2014; 5(3):108.
5. Ahrari F, Mohammadipour HS, Hajimomenian L, Fallah-Rastegar A. The effect of diode laser irradiation associated with photoabsorbing agents containing remineralizing materials on microhardness, morphology and chemical structure of early enamel caries. J Clin Exp Dent. 2018; 10(10):e955-e962.
6. Bahrololoomi Z, Fotuhi Ardakani F, Sorouri M. *In Vitro* Comparison of the Effects of Diode Laser and CO_2 Laser on Topical Fluoride Uptake in Primary Teeth. J Dent (Tehran). 2015; 12(8):585-91.
7. Heravi F, Ahrari F, Mahdavi M, Basafa S. Comparative evaluation of the effect of Er: YAG laser and low-level laser irradiation combined with CPP-ACPF cream on treatment of enamel caries. J Clin Exp Dent. 2014; 6(2):121-6.
8. Zancopé BR, Rodrigues LP, Parisotto TM, Steiner-Oliveira C, Rodrigues LK, Nobre-dos-Santos M. CO_2 laser irradiation enhances CaF_2 formation and inhibits lesion progression on demineralized dental enamel—*In vitro* study. Lasers in medical science. 2016; 31(3):539-47.
9. Rocha CT, Turssi CP, Rodrigues-Júnior AL, Corona SA. Impact of CO_2 laser and stannous fluoride on primary tooth erosion. Lasers in medical science. 2016; 31(3):567-71.
10. Valério RA, Rocha CT, Galo R, Borsatto MC, Saraiva MC, Corona SA. CO_2 laser and topical fluoride therapy in the control of caries lesions on demineralized primary enamel. Scientific World Journal. 2015, 547-569.
11. Poosti M, Ahrari F, Moosavi. The effect of fractional CO_2 laser irradiation on remineralization of enamel white spot lesions. Lasers Med Sci. 2014; 29:1349-1355.
12. Nair AS, Kumar RK, Philip ST, Ahameed SS, Punnathara S, Peter J. A comparative analysis of caries inhibitory effect of remineralizing agents on human enamel treated with Er: YAG Laser: An In-vitro Atomic Emission Spectrometry Analysis. Journal of clinical and diagnostic research: JCDR. 2016; 10(12): ZC10.
13. Moslemi Masume, Fekrazad Reza, Tadayon Nikoo, Ghorbani M, Torabzadeh H, Shadkar M. Effects of Er,Cr:YSGG Laser Irradiation and Fluoride Treatment on Acid Resistance of the Enamel. Pediatric dentistry. 2009; 31:409-13.
14. Asl-Aminabadi N, Najafpour E, Samiei M, Erfanparast L, Anoush S, Jamali Z *et al*. Laser-Casein phosphopeptide effect on remineralization of early enamel lesions in primary teeth. J Clin Exp Dent. 2015; 7(2):e261-7.
15. Chen CC, Huang ST. The effects of lasers and fluoride on the acid resistance of decalcified human enamel. Photomed Laser Surg. 2009; 27(3):447-452.
16. De Sant'Anna GR, dos Santos EA, Soares LE, do Espírito Santo AM, Martin AA *et al*. Dental enamel irradiated with infrared diode laser and photo-absorbing cream: part 2--EDX study. Photomed Laser Surg. 2009; 27(5):771-82.
17. Yassaei S, Shahraki N, Aghili H, Davari A. Combined effects of Er: YAG laser and casein phosphopeptide-amorphous calcium phosphate on the inhibition of enamel demineralization: An *in vitro* study. Dent Res J (Isfahan). 2014; 11(2):193.
18. Castellan C, Ana Claudia Luiz, Leticia Bezinelli M, Roberta Lopes MG, Fausto Mendes M *et al*. *In vitro* evaluation of enamel demineralization after Er:YAG and Nd:YAG laser irradiation on primary teeth. Photomed Laser Surg. 2007; 25(2):85-90.
19. Hemmati S, Dehghan H. Effect of Diode and CO2 Lasers Combined with Sodium Fluoride Varnish on Microhardness of Deciduous Enamel. Journal of Mazandaran University of Medical Sciences. 2016; 26(138):44-54.
20. Souza-Gabriel AE, Colucci V, Turssi CP, Serra MC, Corona SAM. Microhardness and SEM after CO_2 laser irradiation or fluoride treatment in human and bovine enamel. Microsc Res Tech. 2010; 73(11):1030-1035.
21. de Freitas PM, Rapozo-Hilo M, Eduardo C.d P *et al*. *In vitro* evaluation of erbium, chromium:yttrium–scandium–gallium–garnet laser-treated enamel demineralization. Lasers Med Sci. 2010; 25:165-170.
22. Khamverdi Z, Kordestani M, Panahandeh N, Naderi F, Kasraei S. Influence of CO_2 Laser Irradiation and CPPACP Paste Application on Demineralized Enamel Microhardness. J Lasers Med Sci. 2018; 9(2):144-148.
23. Shafer WG, Hine MK, Levy BM Ed. A text book of oral pathology; 5th ed. Philadelphia: WB. Saunders Company, 1993, 567-658.
24. Kalra DD, Kalra RD, Kini PV, Prabhu CA. Nonfluoride remineralization: An evidence-based review of contemporary technologies. Journal of Dental and Allied Sciences. 2014; 3(1):24.
25. Apel C, Meister J, Gotz H, Duschner H, Gutknecht N. Structural changes in human dental enamel after

subablative erbium laser irradiation and its potential use for caries prevention. Caries research. 2005; 39(1):65-70.
26. McCormack SM, Fried D, Featherstone JD, Glena RE, Seka W. Scanning electron microscope observations of CO_2 laser effects on dental enamel. Journal of dental research. 1995; 74(10):1702-8.
27. Sun M, Wu N, Chen H. Laser-assisted rapid mineralization of human tooth enamel. Scientific reports. 2017; 7(1):1-0.