REVISTA DE ODONTOLOGIA DA UNESP
www.revodontolunesp.com.br
Review Article

The biological effects of different LED wavelengths in the health field. A review

Os efeitos biológicos de diferentes comprimentos de onda de LED na área da saúde. Uma revisão

Juliana Cabrini CARMELLO[a], Paula Aboud BARBUGLI[a], Cláudia Carolina JORDÃO[a], Rui OLIVEIRA[b,c,d], Ana Claudia PAVARINA[a]*

[a]UNESP – Universidade Estadual Paulista "Júlio de Mesquita Filho", Departamento de Materiais Odontológicos e Prótese, Araraquara, SP, Brasil
[b]Universidade do Minho, Departamento de Biologia, Centro de Investigação e Tecnologia de Ciências Agroambientais e Biológicas, Gualtar, Braga, Portugal
[c]Universidade do Minho, Departamento de Biologia, Centro de Engenharia Biológica, Gualtar, Braga, Portugal
[d]Universidade do Minho, Departamento de Biologia, Centro de Biologia Molecular e Ambiental, Gualtar, Braga, Portugal

How to cite: Carmello JC, Barbugli PA, Jordão CC, Oliveira R, Pavarina AC. The biological effects of different LED wavelengths in the health field. A review. Rev Odontol UNESP. 2023;52:e20230028. https://doi.org/10.1590/1807-2577.02823

Resumo

Introdução: o uso de diodos emissores de luz ("LED") em vias domésticas e públicas tem aumentado nos últimos 20 anos. Além disso, a luz LED tem sido usada para aplicações médicas. **Objetivo:** pelo fato de seres humanos estarem cada vez mais expostos aos LEDs, há urgência em investigar os possíveis efeitos biológicos nos tecidos causados por esta exposição. Assim, pesquisadores têm focado suas investigações no uso desta luz na área da saúde. **Material e método:** nesta revisão foi realizada uma pesquisa em bancos de dados conceituados sobre os efeitos biológicos causados após aplicação de diferentes protocolos de luz LED em estudos *in vitro* e *in vivo*. **Resultado:** embora a maioria dos artigos publicados tenham mostrado resultados positivos, alguns deles relataram efeitos biológicos negativos da tecnologia de LEDs nas células/tecidos humanos. **Conclusão:** portanto, a compreensão dos efeitos biológicos causados pela luz LED proporcionará uma melhor avaliação dos riscos envolvidos no uso desta tecnologia.

Descritores: Fototerapia; diodo emissor de luz; LED; fontes de luz; efeitos biológicos do LED.

Abstract

Introduction: the use of light emitting diodes (LED) in domestic and public vias have increased in the last 20 years. In addition, the LED light has been used as a light source for medical applications. **Objective:** since humans are increasingly exposed to LEDs, there is an urgency to investigate the possible biological effects on tissues caused by this exposure. So, researchers have been focused their investigations in the application of this light in the health field. **Material and method:** in this review, a search in important databases was performed on the biological effects caused after application of different LED light protocols in *in vitro* and *in vivo* studies. **Result:** although most published papers have shown positive results, some of them reported negative biological effects of light LEDs technology on humans' cells/tissues. **Conclusion:** therefore, the comprehension of the biological effects caused by light LEDs will provide a better assessment of the risks involved using this technology.

Descriptors: Phototherapy; light emitting diode; LED; light sources; LED biological effects.

INTRODUCTION

The search for safe and efficient energy devices has increased over the past 20 years, promoting major improvements in everyday use of equipment such as home appliances and electronics[1]. The lamps are not the exception since the first incandescent lamps such as halogen

and fluorescents had its energy efficacy improved[1]. The light-emitting diode lamps (LED), have been commercialized with significant advantages over conventional devices, because of the internal energy-saving and lifetime that would compensate for the higher prices[1]. Nowadays, the increasing public awareness of environmental concerns has pushed governments and supranational organizations to change the legislation, which regulates the electrical devices[2]. As an example, it was reported that in the European Union, it was imposed a gradual withdrawal of incandescent lamps from the market by replacing them with LEDs (Regulation (EC) n° 244/2009)[2]. In this context, in the future, people will become permanently exposed to LEDs, since these devices will illuminate their houses and the most public and private places. Soon, LED will comprehend at least 50% of the world lighting[3]. Thus, although humans are increasingly exposed to LEDs, the scientific community has been worried about the possible biological effects on tissues caused by this exposure. However, the number of studies performed are scarce.

In the last 15 years, due to a better understanding of photobiology and increased demand for minimally invasive and effective treatments, LEDs have been used for dermatological treatments[1,4]. In the early 1990s, when NASA developed a LED device that allowed its first clinical application[5], the biological effects of LEDs started to be identified[1]. Then, several improvements have been introduced to LED devices resulting in equipment with different wavelengths. These devices have been investigated for their effects on skin cells and, while some studies report an increase in cell proliferation of fibroblasts and keratinocytes, others report disagreeing results on the clinical benefits of using LED on skin wounds[6].

In a recent review, it was described that LED efficacy in photobiomodulation and others healthcare requests are well established and it may have therapeutic applications independent on the wavelength and protocol used[7]. In accordance with the ClinicalTrials.gov database, over 2800 scientific clinical investigations have been made focusing on the possible physiological effects of LED on the most varied parts of the human body, such as brain injury, skin healing, facial rejuvenation, lipolysis, periodontal diseases, temporomandibular disorders, healing of diabetic ulcers, photobiomodulation of Autism Spectrum Disorders (ASD), allergy, and sleeping bruxism[8].

Taken together, it seems that the most of published papers demonstrated positive results in using different protocols and wavelengths of LED on cells or tissues, and the clinical trials that have been made using this device reinforce the idea that LED may be a promising alternative to treat human disorders in the future. Our counterword to this argument is that there are investigations in which protocol and wavelength of LED used were harmful to tissues. For this reason, this review examines the biological effects caused after the application of different LED protocols in the health field. A summary of protocols and wavelengths used is presented in Table 1.

Table 1. Summary finds of data extraction from included articles in the review

LED	Wavelength	Protocol	Associated biological effects	References
RED	630nm	3 applications at fluence of 8J/cm²	Stimulate the human collagen	Barolet et al., 2010[9]
	647nm	applied for 10 s, 30 s or 90 s at fluences of 0.093J/cm², 0.279J/cm² and 0.836J/cm²	Osteogenic differentiation	Kim et al., 2009[10]
	633nm	1 application at fluence of 0.5, 1.0, 1.5 and 2.0 J/cm²	Effect in human marrow stromal fibroblast cells: altered the gene expression related to cell proliferation, osteogenic potential, adipogenesis, mRNA and protein content.	Guo et al., 2015[11]
	633nm	2 sessions a week for 4 weeks – 126J/cm²	Skin and mucosal wound healing, skin rejuvenation	Lee et al., 2007[12]
	670nm	Daily treatment for 14 days using a fluence of 4 J/cm²	Treatment of precancerous lesions, warts, pain attenuation of oral mucositis	Whelan et al., 2002[13]
	645nm	3 times a day for 1 week at fluence of 0.99 J/cm²	Relief in the oral mucositis	Corti et al., 2006[14]
	660nm	5, 6 or 10 sessions for 1 to 3 weeks using a fluence of 5J/cm²	Treatment of polymorphous light eruption	Barolet, Boucher, 2008[15]
	660nm	3 applications a week for 4 weeks (fluence not mentioned)	Skin rejuvenation	Barolet et al., 2009[16]
	660nm	1 session a day for 12 weeks using a fluence of 5.17J/cm²	Treatment of wrinkles	Nam et al., 2017[17]
	660nm	1 session at fluence of 10 J/cm² for 7 days	Induction of angiogenesis	Sousa et al., 2013[18]

Table 1. Continued...

LED	Wavelength	Protocol	Associated biological effects	References
Blue	412, 419 and 426 nm	66 to 100 J/cm²	Inhibited skin keratinocytes proliferation and altered cell differentiation	Liebmann et al., 2010[19]
	430-490nm	Applications for 20, 40, 80 and 120 s at a fluence of 8, 14 and 15J/cm²	Reduction of mitotic activity of dermal fibroblasts	Malčić et al., 2012[20] and Lev-Tov et al., 2013[21]
	420nm	15 and 30J/cm²	Decrease cell differentiation of dermal fibroblasts	Taflinski et al., 2014[22]
	411nm	Fluence not mentioned	Apoptosis of human retinal cells	Knells et al., 2011[23]
	465nm	10 min/day for 5 days at fluences of 9 and 18J/cm²	Apoptosis of human colon cancer cells	Matsumoto et al., 2014[24]
	470nm	72 J/cm², 144 J/cm², 216 J/cm² and 288 J/cm²	Reduced human colorectal cancer cells	Yan et al., 2018[25]
	Not mentioned	162 J/cm²	Inhibited of gingival fibroblast proliferation	Taoufik et al., 2008[26]
	Not mentioned	198J/cm² for 72 h	Apoptosis of intestine cells of neonatal rats	Tanaka et al., 2008[27]
	460nm	1 session at fluence of 10 J/cm² for 7 days	Did not induce angiogenesis	Sousa et al., 2013[18]
	400-500nm	Patients were exposed for at least 12 h. Fluence not mentioned	DNA damage of mononuclear leukocytes and decreased the blood flow in blood vessels in jaundiced neonates	Benders et al., 1999[28] Aycicek, Erel, 2007[29]
	400nm	Light intensity of 200 Lux for 10 seconds	Damage on retinal cells	Ortín-Martínez et al., 2014[30]
	455-465nm	Light intensity of 500 Lux	Damage on retinal cells	Krigel et al., 2016[31]
	460nm	Light intensity of 150 Lux for 3h per day for 21 days	Toxicity for retinal pigment epithelial cells	Lin et al., 2019[32]
	455-495nm	Review	Retina damage	Tosini et al., 2016[33]
	455-495nm	Review	Inhibition of superoxide dismutase and catalase. Toxicity for retinal pigment epithelial cells	Tokarz et al., 2013[34]
Yellow	570-590 nm	250 milliseconds at fluence of 0.1 J/cm² for 4, 8, 12, 18 weeks and 6 and 12 months	Collagen synthesis, skin texture improvement	McDaniel et al., 2002[35] and Weiss et al., 2005[36]
	570-590 nm	100 pulses, 250 milliseconds per pulse at fluence of 0.15 J/cm²	Decrease the incidence of dermatitis	DeLand et al., 2007[37]
	590 nm	0.1 J/cm²	Increased collagen I production and decreased collagenase (MMP-1)	McDaniel et al., 2010[38]
White	411-777 nm	CCTs equivalent to 2954, 5624, and 7378 K for 8h/16h	Toxic for lens epithelial cells	Xie et al., 2014[3]
	411-777 nm	Illumination of animals with 6000 lux, 1500, 1000 and 500 lux for 1 week and 1 month	Toxic for lens epithelial cells	Krigel et al., 2016[31]
	411-777 nm	Illumination of animals at constant light for 6, 12, 18, 24, 48, and 72 h	Toxic for retinal cells, loss of photoreceptors and the activation of caspase-independent apoptosis, necroptosis, and necrosis	Jaadane et al., 2015[39]
	411-777 nm	5.17 J/cm²	Improved periocular wrinkles	Nam et al., 2017[40]

min: minutes; seg: seconds; h: hour.

Red LED - 630-700 nm

In accordance with the literature, the red LEDs (630-700 nm) are known to permit the penetration of light deeper into tissues when compared to other LEDs with different wavelengths, so, they are used to reach adjacent skin structures and also the connective tissue[41]. For this reason, the search for protocols that allow the treatment of the most varied health problems has been the target of some investigations[9-11]. It has been reported that three applications of short and intermittent light delivery (red LED (630 nm) at a light dose of 8 J/cm², seems to stimulate the human collagen production *in vitro*[9]. In another investigation, it has been reported that red light, when used at 647 nm wavelength, applied for 10 s, 30 s or 90 s at light doses of 0.093 J/cm², 0.279 J/cm² and 0.836 J/cm², respectively, may promote the osteogenic differentiation in mesenchymal cells[10]. In addition, it has been reported that red LED (633 nm) altered the gene expression related to cell proliferation, osteogenic potential, adipogenesis, mRNA and protein content, in human marrow stromal fibroblast cells when irradiated at a light doses equivalent to 0.5, 1.0, 1.5 and 2.0 J/cm²[2,11].

In the clinical field, many protocols for using red LEDs devices have been studied including skin and mucosal wound healing, skin rejuvenation[12], treatment of precancerous lesions, warts, pain attenuation of oral mucositis[13], postoperative pain and edema[42]. Corti et al.[14], using a red

LED device (645 nm) with an output delivery equivalent to 7.8 mW/cm^2 and a dose of light of 0.99 J/cm^2, three times a day for 1 week, observed a relief in the oral mucositis present in patients underwent to chemotherapy[14]. Another investigation reported the efficacy of phototherapy using red LED (660 mn) in the treatment of polymorphous light eruption (PLE). The patients presented a reduction in the skin erythema, after 5, 6 or 10 sessions of treatment during 1 to 3 weeks. It was used equipment with an output delivery of 60 mW/cm^2 and a dose of light equivalent to 5 J/cm^2[2,15]. Barolet et al.[16] demonstrated that the red LED at 660 mn can be a good choice to promote skin rejuvenation using *in vitro* and *in vivo* evaluation. In the *in vitro* assay, the authors used a Human Reconstructed Skin tissue (HRS) and applied 11 sequentially pulsed treatments of red LED for 4 weeks. For the *in vivo* study, patients received 12 applications of red LED being 3 treatments a week, for 4 weeks. Authors suggested that improvements in the skin of patients are justified by the upregulation of the collagen and downregulation of MMP-1, a gene encoding interstitial collagenase. However, details of the dose of light, time of application of each treatment and the output of the LED device were not mentioned[16]. Recently, a clinical trial was performed for the treatment of wrinkles. The faces of 52 female patients, were irradiated daily, with 5.17 J/cm^2 with red LED (660 nm) for 12 weeks and it was observed that red LED was the most successful protocol when compared to the LED wavelengths equivalent to 411 nm and 777 nm[17]. Additionally, it has been reported the capacity of red LED to induce angiogenesis on dorsal wounds after illumination, using a device with 15 mW and light dose of 10 J/cm^2 in rats. The protocol was applied once a day for 7 days and it promoted a significant increase in angiogenesis[18].

The photobiomodulation therapy offers a non-invasive, safe, drug-free, and side-effect-free method for pain relief of both acute and chronic musculoskeletal conditions as well as fibromyalgia[43]. When a super-pulsed laser (905 nm) combined with red (640 nm) and infrared (875 nm) light-emitting diodes, was used, it was observed that pain intensity decreased significantly, with a median decrease of 2.2 - 2.7 pain points on a 10-point scale and this decrease in pain was maintained for 48 h post treatment[44].

As can be seen, the protocols using red LED promoted a reduction of oral mucositis and skin lesions, increased angiogenesis and were efficient for skin rejuvenation. Besides, it has been reported an increase in cell proliferation of various cell types such as fibroblasts, endothelial cells, and keratinocytes. However, the biological mechanisms that justify the light actions of low intensity in tissues have not been elucidated.

Blue LED – 400-470 nm

It has been reported that the irradiation with blue LEDs (412, 419 and 426 nm) using a dose of light from 66 to 100 J/cm^2 inhibited the proliferation of skin keratinocytes and altered cell differentiation[19]. Likewise, in other investigations, dermal fibroblasts demonstrated reduced mitotic activity after exposure to blue LED (430-490 nm) for 20, 40, 80 and 120 seconds at a dose of light of 8, 14 and 15 J/cm^2[20,21]. Taflinski et al.[22], observed that human dermal fibroblasts exhibited a decrease in cell differentiation when irradiated with blue LED (420 nm), with an intensity of 50 mW/cm^2 and a dose of light of 15 and 30 J/cm^2. Human retinal cells have also been affected by blue LED irradiation[23]. In an *in vitro* investigation, when human retinal cells were exposed to LED at 411 nm with an intensity of 0.6, 1.5 and 4.5 W/m^2 and 470 nm with an intensity of 4.5 W/m^2 was verified a cytotoxic effect of LED at 411 nm with the intensity of 4.5W/m^2, which induced the retinal cells to apoptosis[23]. In addition, it has been reported the anti-proliferative effect of blue LED in cancer cells of the human colon by induction of the extrinsic apoptotic pathway[24]. Recently, another *in vitro* study reported that the blue LED (470 nm) used at doses of 72 J/cm^2, 144 J/cm^2, 216 J/cm^2, and 288 J/cm^2, reduced proliferation of human colorectal cancer cells[25].

In the dental field, the blue LED when applied with an intensity of 900 mW/cm^2 and a dose of light equivalent to 162 J/cm^2, inhibited the proliferation of gingival fibroblasts[26]. In another study,

the blue LED was also applied to verify the viability and synthesis of dentin matrix proteins by odontoblast-like cells. The protocol used consisted in a single application using equipment with an intensity of 20 mW/cm and a dose of light equivalent to 0.5, 2, 4, 10, or 15 J/cm^2 and it was observed that blue LED did not present bio stimulatory capacity on odontoblast-like cells[45].

In an *in vivo* study it was demonstrated that the blue LED device induced intestine cells of neonatal rats to apoptosis when applied in an intensity of 55 mW/cm^2 for 72 hours[27]. Another *in vivo* investigation verified that the blue LED (460 nm) did not stimulate angiogenesis on dorsal cutaneous wounds. It was performed one application per day for 7 days using a device with an intensity of 22 mW and dose of light of 10 J/cm[18]. Moreover, some *in vivo* investigations reported the genotoxicity of blue LED to mononuclear leukocytes and decreased the blood flow in blood vessels in jaundiced neonates[28,29,46-50].

Similarly, to other areas, the investigations about the effects of blue LED in the ophthalmology field have increased[30,31]. An *in vivo* investigation reported the phototoxicity effect of blue LED (400 nm) on retinal cells of rats, using an intensity equivalent to 200 Lux for 10 seconds[30]. In another investigation, it was observed that the blue LED (455-465 nm) may cause retinal toxicity in rats, after illumination of 500 Lux, which is the domestic classic light intensity[31]. An *in vivo* study revealed that blue LED at 460 nm, was toxic for retinal pigment epithelial cells[32]. The authors illuminated rats with an intensity of 150 Lux for 3 h per day for 21 days and verified that the light caused fundus damage, decreased total retinal thickness, and caused neuron transduction injury in the retina[32]. It has also been documented that the degeneration of the pigment epithelium under blue light is promoted by the accumulation of A2E (bis-retinoid N-retinyl-N-retinylidene ethanolamine), but this effect does not show significant disturbances[51].

In general, while only one investigation reported the benefits of using blue LEDs, in the inhibition of mitotic activity of cancer cells of the human colon[24], other investigations observed that different protocols using this LED may cause apoptosis in intestine cells of rats[27] and human retinal cells[30-32]. Regarding the retinal cells, it was demonstrated that independently on the protocol of illumination used, the association between blue light and chronic retinal degeneration was verified[33]. Short-wavelength blue light (455 nm to 495 nm) is characterized as high-energy radiation in the visible spectrum and is easily transmitted to the lens, directly causing damage to the retina[33]. In addition, it was also reported that blue light inhibited the activity of superoxide dismutase and catalase[34] and induced the retinal pigment epithelium cells to death[34]. Exposure to artificial light at night is a new source of pollution, because it affects the circadian clock and consequently, the secretion of melatonin and estrogen[52]. This topic is an important issue and needs to be emphasized since people are daily exposed to this type of light in their electronic products such as smartphones, tablets, and computers[52,53].

Yellow LED 570-590 nm

Beyond the red and blue LEDs, previous investigations have reported the photobiomodulation caused by Yellow LED (570 - 590 nm)[35,36]. In these investigations, several protocols were developed, and the authors verified that the collagen synthesis was related to the clinical alterations found in human skin, including a lower production of some metalloproteinases[35]. Based on the results, one protocol was defined (irradiations of 250 milliseconds with a dose of light of 0.1 J/cm^2 and the output delivery of 4.0 mW/cm^2) and used for 4, 8, 12, 18 weeks and 6 and 12 months. The authors observed the improvement of the skin texture of 90 patients treated with yellow LED[36]. In another study, it was observed that the photobiomodulation caused by yellow LED was efficient to decrease the incidence of dermatitis in patients with breast cancer[37]. The patients were treated by application of 100 pulses, 250 milliseconds per pulse at a dose of light of 0.15 J/cm^2,[37]. McDaniel et al.[38], to upgrade the achieved clinical results, conducted an *in vitro* investigation combining the yellow LED with infra-red LED (590/870 nm). The output

delivery used was equivalent to 4.0 mW/cm^2 and the dose of light was equivalent to 0.1 J/cm ^{2}. Authors observed a significant increase in collagen I and decrease in collagenase[38]. When the LED (590 nm) was evaluated in cells, it inhibited human microvascular endothelial cells migration, vascular endothelial growth factor and stem cell factor, being a novel therapeutic option for treat melasma[54]. It is important to notice that, since this type of light has photobiomodulation activity on human tissues, the number of investigations that used the yellow LED is scarce. Therefore, since these treatments yielded relevant results, further studies are necessary to clarify the effect of yellow LED on biological tissues.

White LED 411-777 nm

The photobiological effects of white LED on human cells were also evaluated[3] and considering the optical characteristics, white LEDs may be quite diverse due to the different manufacturing techniques of the equipment. As a better description of the spectral characteristics of the white LED, the photobiological effects of the correlated color temperature (CCT) of white LED on cultured human corneal epithelial cells has been evaluated. Cells were irradiated with white LED with CCTs equivalent to 2954, 5624, and 7378 K. The irradiation was performed for 8 h/16 h, to mimic our daily routine. The results showed that LEDs increased the production of intracellular ROS and were genotoxic, both in a dose-dependent manner. Thus, white LED toxicity for lens epithelial cells was also directly dependent CCT[3]. In another investigation, commercially available white LEDs and four different blue LEDs (507, 473, 467, and 449 nm) were used for exposure of retinal cells of rats. Animals were exposed to constant light for 6, 12, 18, 24, 48, and 72 h, and it was verified a loss of photoreceptors and the activation of caspase-independent apoptosis, necroptosis, and necrosis[39]. A recent report demonstrated that the blue component of white-LED caused retinal toxicity in albino rats[40]. These results were observed after 24 hours of exposure at different light intensities (6000 lux, 1500, 1000 and 500 lux)[31]. In contrast, white LED (411-777 nm) when applied at a dose of light of 5.17 J/cm^2 was able to improve the periocular wrinkles of female patients[40]. The oxidative stress activates multiple signaling pathways including mitogen-activated protein kinase cascades that are responsible to causes retinal pigment epithelium damage[55].

As commented previously, the blue component of white light seems to be the main responsible for its toxicity. Taking into consideration that white LED is the most used light in domestic lighting, public and private roads, their widespread use needs to be reassessed.

The Action of LEDs on Cells

In general, it has been suggested that the cytotoxicity of LEDs is related to the increase of cell apoptosis, production of reactive oxygen species (ROS), lipid peroxidation and DNA damage[3,55]. Mitochondria have also been identified as a target for the toxicity of LED illumination[15,23,56,57], which could be related to the induction of apoptosis. It is known that the mitochondria, a fundamental organelle for maintaining vital cellular functions, also plays a key role in cell death through the regulation of cytochromes[58,59], intracellular Ca^{2+} concentration[59], reactive oxygen species (ROS)[60-62], transmembrane mitochondrial potential[63], mitochondrial transition pores by caspases or ATP depletion[62], changes in the redox state metabolism[64] and cyclosporine A-sensitive mitochondrial permeability transition[62]. The irradiation by LED is absorbed by mitochondrial chromophores, including cytochrome c oxidase[1]. Irradiation affects the mitochondrial respiratory chain by changing the electrical power of cellular membranes and, consequently, the selective permeability of sodium, potassium, and calcium ions or through increased activity of enzymes, such as cytochrome c oxidase and ATP synthase[63,65]. In addition, it has been reported an increase in the mitochondrial respiration in the respiratory control state of rat liver cells, after irradiation with LED at 650 nm in a dose of 3 J/cm^2 or higher[66]. On the other hand, the same research group found a decrease of mitochondrial respiration of rat liver cells, in

the phosphorylating state, after irradiation using the same red LED and doses of light. They demonstrated that the cytochrome c oxidase is important in the photoreactivation of mitochondrial activity blocked by nitric oxide[57]. Therefore, according to the results of these studies the alteration caused by LED on the mitochondrial level is still controversial.

Concerning the DNA damage, it is important to note that DNA damage would be expected as a consequence of mitochondrial impairment and ROS production caused by LED irradiation independently of the wavelength used[25]. However, reports on genotoxicity are scarce and sometimes contradictory[25,55,67]. Considering that these radiations may promote DNA modifications, they can become potentially mutagenic and cause malignancy in human cells, so, this aspect should be explored in the future. Moreover, the effects that LED may cause human cells is dependent on the wavelength, the intensity of the LED device, the distance between the equipment and the cells irradiated, energy delivered per surface area and the exposure time employed for each protocol used. Each color of light or wavelength presents different penetration depths on biological tissues, beyond each biological effect related to differences in chromophore targets[4,68].

Relevant Considerations

In the present review, it is important to mention the ICNIRP Guideline, 2013 (International Commission on non-ionizing radiation protection), which describes the principles of protection against laser radiation hazards, in parallel to the exposure to non-laser optical radiation[69]. In accordance with ICNIRP, shorter-wavelength visible radiation in the region from 400 nm to 550 nm (blue light region), has been suggested to damage the retina, for lasers and non-laser radiation[70-72]. Thus, based in these observations one can assume that the harmful effects caused by LED radiation would be reproduced by laser radiation, just using the same power and wavelength of light. However, the guideline suggests that the safety limits of exposure for laser and non-laser sources, such as the sun, tungsten filaments xenon lamps, and LEDs, may be different[69]. These differences might be related to the nature of each radiation, for instance, the controlled or non-controlled emission of photons and also the type of beam produced by the light source such as the case of the laser beam, which is well collimated, while LED beam is not collimated[69]. As the exposure limits also depend on the irradiance diameter (spot size), a collimated beam is more conservative than the non-collimated counterpart, in the context of light safety exposure.

As for the emission spectrum, it has been reported that LED devices is constituted of blue radiations or blue components, known to be potentially dangerous to the retina. It was verified that the blue components cause retinal toxicity at occupational domestic illuminance and not only under experimental conditions[31]. So, the biological effects reported here, allow us to question the safeness of the LED radiation. It is possible to suggest that the effects produced by the LED devices, are related not only to the power or wavelength of LED device but also to the nature of the light radiation. Taking together, these arguments reinforce the idea that the nature of light can be another factor to cause adverse effects on biological tissues.

CONCLUSION

In summary, the phototherapy seems to be a promising alternative to treat a varied range of diseases. However, the results described in the literature are inconsistent, mainly due to the lack of methodological standardization of the studies. It is important to state that most investigations were performed based on acute light exposure and do not take into account the effects of prolonged exposures on timescales of weeks, months, and years to mimic human daily routine[31,69]. Therefore, the comprehension of biological effects caused by repeated exposure of LEDs will provide a better assessment of risks involved using this technology. These data would be of extreme importance to manufacturers of light devices to improve the safeness and eliminate the harmful effects of LED irradiation.

ACKNOWLEDGMENTS

This work was supported by São Paulo Research Foundation (FAPESP), Brazil (grants numbers #2013/07276-1, #2016/13868-7 and # 2017/02559-6).

REFERENCES

1. Chaves MEA, Araújo AR, Piancastelli ACC, Pinotti M. Effects of low-power light therapy on wound healing: LASER x LED. An Bras Dermatol. 2014 Jul-Aug;89(4):616-23. http://dx.doi.org/10.1590/abd1806-4841.20142519. PMid:25054749.
2. Behar-Cohen F, Martinsons C, Viénot F, Zissis G, Barlier-Salsi A, Cesarini JP, et al. Light-emitting diodes (LED) for domestic lighting: any risks for the eye? Prog Retin Eye Res. 2011 Jul;30(4):239-57. http://dx.doi.org/10.1016/j.preteyeres.2011.04.002. PMid:21600300.
3. Xie C, Li X, Tong J, Gu Y, Shen Y. Effects of white light-emitting diode (LED) light exposure with different correlated color temperatures (CCTs) on human lens epithelial cells in culture. Photochem Photobiol. 2014 Jul-Aug;90(4):853-9. http://dx.doi.org/10.1111/php.12250. PMid:24483628.
4. Jagdeo J, Austin E, Mamalis A, Wong C, Ho D, Siegel DM. Light-emitting diodes in dermatology: a systematic review of randomized controlled trials. Lasers Surg Med. 2018 Jan;50(6):613-28. http://dx.doi.org/10.1002/lsm.22791. PMid:29356026.
5. Calderhead RG. The photobiological basics behind light-emitting diode (LED) phototherapy. Laser Ther. 2007 Jan;16(2):97-108. http://dx.doi.org/10.5978/islsm.16.97.
6. Opel DR, Hagstrom E, Pace AK, Sisto K, Hirano-Ali SA, Desai S, et al. Light-emitting diodes: a brief review and clinical experience. J Clin Aesthet Dermatol. 2015 Jun;8(6):36-44. PMid:26155326.
7. Heiskanen V, Hamblin MR. Photobiomodulation: lasers vs. light emitting diodes? Photochem Photobiol Sci. 2018 Aug;17(8):1003-17. http://dx.doi.org/10.1039/c8pp00176f. PMid:30044464.
8. ClinicalTrials.gov. FDAAA 801 and the final rule [Internet]. Bethesda: ClinicalTrials.gov; 2023 [cited 2023 Oct 26]. Available from: http://clinicaltrials.gov/ct2/manage-recs/fdaaa
9. Barolet D, Duplay P, Jacomy H, Auclair M. Importance of pulsing illumination parameters in low-level-light therapy. J Biomed Opt. 2010 Jul-Aug;15(4):048005. http://dx.doi.org/10.1117/1.3477186. PMid:20799848.
10. Kim HK, Kim JH, Abbas AA, Kim DO, Park SJ, Chung JY, et al. Red light of 647 nm enhances osteogenic differentiation in mesenchymal stem cells. Lasers Med Sci. 2009 Mar;24(2):214-22. http://dx.doi.org/10.1007/s10103-008-0550-6. PMid:18386092.
11. Guo J, Wang Q, Wai D, Zhang QZ, Shi SH, Le AD, et al. Visible red and infrared light alters gene expression in human marrow stromal fibroblast cells. Orthod Craniofac Res. 2015 Apr;18(Suppl 1):50-61. http://dx.doi.org/10.1111/ocr.12081. PMid:25865533.
12. Lee SY, Park KH, Choi JW, Kwon JK, Lee DR, Shin MS, et al. A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings. J Photochem Photobiol B. 2007 Jul;88(1):51-67. http://dx.doi.org/10.1016/j.jphotobiol.2007.04.008. PMid:17566756.
13. Whelan HT, Connelly JF, Hodgson BD, Barbeau L, Post AC, Bullard G, et al. NASA light-emitting diodes for the prevention of oral mucositis in pediatric bone marrow transplant patients. J Clin Laser Med Surg. 2002 Dec;20(6):319-24. http://dx.doi.org/10.1089/104454702320901107. PMid:12513918.
14. Corti L, Chiarion-Sileni V, Aversa S, Ponzoni A, D'Arcais R, Pagnutti S, et al. Treatment of chemotherapy-induced oral mucositis with light-emitting diode. Photomed Laser Surg. 2006 Apr;24(2):207-13. http://dx.doi.org/10.1089/pho.2006.24.207. PMid:16706701.

15. Barolet D, Boucher A. LED photoprevention: reduced MED response following multiple LED exposures. Lasers Surg Med. 2008 Feb;40(2):106-12. http://dx.doi.org/10.1002/lsm.20615. PMid:18306161.

16. Barolet D, Roberge CJ, Auger FA, Boucher A, Germain L. Regulation of skin collagen metabolism in vitro using a pulsed 660 nm LED light source: clinical correlation with a single-blinded study. J Invest Dermatol. 2009 Dec;129(12):2751-9. http://dx.doi.org/10.1038/jid.2009.186. PMid:19587693.

17. Nam CH, Park BC, Kim MH, Choi EH, Hong SP. The efficacy and safety of 660 nm and 411 to 777 nm light-emitting devices for treating wrinkles. Dermatol Surg. 2017 Mar;43(3):371-80. http://dx.doi.org/10.1097/DSS.0000000000000981. PMid:28195844.

18. Sousa AP, Paraguassú GM, Silveira NT, Souza J, Cangussú MC, Santos JN, et al. Laser and LED phototherapies on angiogenesis. Lasers Med Sci. 2013 May;28(3):981-7. http://dx.doi.org/10.1007/s10103-012-1187-z. PMid:22923269.

19. Liebmann J, Born M, Kolb-Bachofen V. Blue-light irradiation regulates proliferation and differentiation in human skin cells. J Invest Dermatol. 2010 Jan;130(1):259-69. http://dx.doi.org/10.1038/jid.2009.194. PMid:19675580.

20. Malčić AI, Pavičić I, Trošić I, Simeon P, Katanec D, Krmek SJ. The effects of bluephase LED light on fibroblasts. Eur J Dent. 2012 Jul;6(3):311-7. http://dx.doi.org/10.1055/s-0039-1698966. PMid:22904660.

21. Lev-Tov H, Mamalis A, Brody N, Siegel D, Jagdeo J. Inhibition of fibroblast proliferation in vitro using red light-emitting diodes. Dermatol Surg. 2013 Aug;39(8):1167-70. http://dx.doi.org/10.1111/dsu.12212. PMid:23590233.

22. Taflinski L, Demir E, Kauczok J, Fuchs PC, Born M, Suschek CV, et al. Blue light inhibits transforming growth factor-β1-induced myofibroblast differentiation of human dermal fibroblasts. Exp Dermatol. 2014 Apr;23(4):240-6. http://dx.doi.org/10.1111/exd.12353. PMid:24533842.

23. Knels L, Valtink M, Roehlecke C, Lupp A, de la Vega J, Mehner M, et al. Blue light stress in retinal neuronal (R28) cells is dependent on wavelength range and irradiance. Eur J Neurosci. 2011 Aug;34(4):548-58. http://dx.doi.org/10.1111/j.1460-9568.2011.07790.x. PMid:21781192.

24. Matsumoto N, Yoshikawa K, Shimada M, Kurita N, Sato H, Iwata T, et al. Effect of light irradiation by light emitting diode on colon cancer cells. Anticancer Res. 2014 Sep;34(9):4709-16. PMid:25202048.

25. Yan G, Zhang L, Feng C, Gong R, Idiiatullina E, Huang Q, et al. Blue light emitting diodes irradiation causes cell death in colorectal cancer by inducing ROS production and DNA damage. Int J Biochem Cell Biol. 2018 Oct;103:81-8. http://dx.doi.org/10.1016/j.biocel.2018.08.006. PMid:30125666.

26. Taoufik K, Mavrogonatou E, Eliades T, Papagiannoulis L, Eliades G, Kletsas D. Effect of blue light on the proliferation of human gingival fibroblasts. Dent Mater. 2008 Jul;24(7):895-900. http://dx.doi.org/10.1016/j.dental.2007.10.006. PMid:18164382.

27. Tanaka K, Hashimoto H, Tachibana T, Ishikawa H, Ohki T. Apoptosis in the small intestine of neonatal rat using blue light-emitting diode devices and conventional halogen-quartz devices in phototherapy. Pediatr Surg Int. 2008 Jul;24(7):837-42. http://dx.doi.org/10.1007/s00383-008-2170-4. PMid:18470518.

28. Benders MJ, Van Bel F, Van de Bor M. Cardiac output and ductal reopening during phototherapy in preterm infants. Acta Paediatr. 1999 Sep;88(9):1014-9. http://dx.doi.org/10.1111/j.1651-2227.1999.tb00199.x. PMid:10519346.

29. Aycicek A, Erel O. Total oxidant/antioxidant status in jaundiced newborns before and after phototherapy. J Pediatr. 2007 Jul-Aug;83(4):319-22. http://dx.doi.org/10.2223/JPED.1645. PMid:17625638.

30. Ortín-Martínez A, Valiente-Soriano FJ, García-Ayuso D, Alarcón-Martínez L, Jiménez-López M, Bernal-Garro JM, et al. A novel in vivo model of focal light emitting diode-induced cone-photoreceptor phototoxicity: neuroprotection afforded by brimonidine, BDNF, PEDF or bFGF. PLoS One. 2014 Dec;9(12):e113798. http://dx.doi.org/10.1371/journal.pone.0113798. PMid:25464513.

31. Krigel A, Berdugo M, Picard E, Levy-Boukris R, Jaadane I, Jonet L, et al. Light-induced retinal damage using different light sources, protocols and rat strains reveals LED phototoxicity. Neuroscience. 2016 Dec;339:296-307. http://dx.doi.org/10.1016/j.neuroscience.2016.10.015. PMid:27751961.

32. Lin CH, Wu MR, Huang WJ, Chow DS, Hsiao G, Cheng YW. Low-luminance blue light-enhanced phototoxicity in A2E-Laden RPE cell cultures and rats. Int J Mol Sci. 2019 Apr;20(7):1799. http://dx.doi.org/10.3390/ijms20071799. PMid:30979028.

33. Tosini G, Ferguson I, Tsubota K. Effects of blue light on the circadian system and eye physiology. Mol Vis. 2016 Jan;22:61-72. PMid:26900325.

34. Tokarz P, Kaarniranta K, Blasiak J. Role of antioxidant enzymes and small molecular weight antioxidants in the pathogenesis of age-related macular degeneration (AMD). Biogerontology. 2013 Oct;14(5):461-82. http://dx.doi.org/10.1007/s10522-013-9463-2. PMid:24057278.

35. McDaniel DH, Weiss RA, Geronemus R, Ginn L, Newman J. Light–tissue interactions I: photothermolysis versus photomodulation laboratory findings. Lasers Surg Med. 2002 Jan;14:25.

36. Weiss RA, McDaniel DH, Geronemus RG, Weiss MA. Clinical trial of a novel non-thermal LED array for reversal of photoaging: clinical, histologic, and surface profilometric results. Lasers Surg Med. 2005 Feb;36(2):85-91. http://dx.doi.org/10.1002/lsm.20107. PMid:15654716.

37. DeLand MM, Weiss RA, McDaniel DH, Geronemus RG. Treatment of radiation-induced dermatitis with light-emitting diode (LED) photomodulation. Lasers Surg Med. 2007 Feb;39(2):164-8. http://dx.doi.org/10.1002/lsm.20455. PMid:17311276.

38. McDaniel DH, Weiss RA, Geronemus RG, Mazur C, Wilson S, Weiss MA. Varying ratios of wavelengths in dual wavelength LED photomodulation alters gene expression profiles in human skin fibroblasts. Lasers Surg Med. 2010 Aug;42(6):540-5. http://dx.doi.org/10.1002/lsm.20947. PMid:20662030.

39. Jaadane I, Boulenguez P, Chahory S, Carré S, Savoldelli M, Jonet L, et al. Retinal damage induced by commercial light emitting diodes (LEDs). Free Radic Biol Med. 2015 Jul;84:373-84. http://dx.doi.org/10.1016/j.freeradbiomed.2015.03.034. PMid:25863264.

40. Nam CH, Park BC, Kim MH, Choi EH, Hong SP. The efficacy and safety of 660 nm and 411 to 777 nm light-emitting devices for treating wrinkles. Dermatol Surg. 2017 Mar;43(3):371-80. http://dx.doi.org/10.1097/DSS.0000000000000981. PMid:28195844.

41. Simpson CR, Kohl M, Essenpreis M, Cope M. Near-infrared optical properties of ex vivo human skin and subcutaneous tissues measured using the Monte Carlo inversion technique. Phys Med Biol. 1998 Sep;43(9):2465-78. http://dx.doi.org/10.1088/0031-9155/43/9/003. PMid:9755939.

42. Kim WS, Calderhead RG. Is light-emitting diode phototherapy (LED-LLLT) really effective? Laser Ther. 2011;20(3):205-15. http://dx.doi.org/10.5978/islsm.20.205. PMid:24155530.

43. Oliveira MF, Johnson DS, Demchak T, Tomazoni SS, Leal-Junior EC. Low-intensity LASER and LED (photobiomodulation therapy) for pain control of the most common musculoskeletal conditions. Eur J Phys Rehabil Med. 2022 Apr;58(2):282-9. http://dx.doi.org/10.23736/S1973-9087.21.07236-1. PMid:34913330.

44. Herpich CM, Leal-Junior ECP, Politti F, Gomes CAFP, Glória IPS, Amaral MFRS, et al. Intraoral photobiomodulation diminishes pain and improves functioning in women with temporomandibular disorder: a randomized, sham-controlled, double-blind clinical trial. Lasers Med Sci. 2020 Mar;35(2):439-45. http://dx.doi.org/10.1007/s10103-019-02841-1. PMid:31325122.

45. Alonso JR, Turrioni AP, Basso FG, Costa CAS, Hebling J. Synthesis of dental matrix proteins and viability of odontoblast-like cells irradiated with blue LED. Lasers Med Sci. 2016 Apr;31(3):523-30. http://dx.doi.org/10.1007/s10103-016-1889-8. PMid:26873499.

46. Kadalraja R, Patole SK, Muller R, Whitehall JS. Is mesenteric blood flow compromised during phototherapy in preterm neonates? Arch Dis Child Fetal Neonatal Ed. 2004 Nov;89(6):F564. http://dx.doi.org/10.1136/adc.2004.057646. PMid:15499160.

47. Dennery PA, Lorch S. Neonatal blue-light phototherapy could increase the risk of dysplastic nevus development. Pediatrics. 2007;120(1):247-8. http://dx.doi.org/10.1542/peds.2007-0844. PMid:17606593.

48. Furchgott RF. Endothelium-dependent relaxation, endothelium-derived relaxing factor and photorelaxation of blood vessels. Semin Perinatol. 1991 Feb;15(1):11-5. PMid:2063224.

49. Wu PY, Wong WH, Hodgman JE, Levan N. Changes in blood flow in the skin and muscle with phototherapy. Pediatr Res. 1974 Apr;8(4):257-62. http://dx.doi.org/10.1203/00006450-197404000-00007. PMid:4822668.

50. Aycicek A, Kocyigit A, Erel O, Senturk H. Phototherapy causes DNA damage in peripheral mononuclear leukocytes in term infants. J Pediatr. 2008;84(2):141-6. http://dx.doi.org/10.2223/JPED.1765. PMid:18350230.

51. Alaimo A, Liñares GG, Bujjamer JM, Gorojod RM, Alcon SP, Martínez JH, et al. Toxicity of blue led light and A2E is associated to mitochondrial dynamics impairment in ARPE-19 cells: implications for age-related macular degeneration. Arch Toxicol. 2019 May;93(5):1401-15. http://dx.doi.org/10.1007/s00204-019-02409-6. PMid:30778631.

52. Touitou Y, Point S. Effects and mechanisms of action of light-emitting diodes on the human retina and internal clock. Environ Res. 2020 Nov;190:109942. http://dx.doi.org/10.1016/j.envres.2020.109942. PMid:32758719.

53. O'Hagan JB, Khazova M, Price LL. Low-energy light bulbs, computers, tablets and the blue light hazard. Eye. 2016 Feb;30(2):230-3. http://dx.doi.org/10.1038/eye.2015.261. PMid:26768920.

54. Dai X, Jin S, Xuan Y, Yang Y, Lu X, Wang C, et al. 590 nm LED irradiation improved erythema through inhibiting angiogenesis of human microvascular endothelial cells and ameliorated pigmentation in melasma. Cells. 2022 Dec;11(24):3949. http://dx.doi.org/10.3390/cells11243949. PMid:36552713.

55. Chamorro E, Bonnin-Arias C, Pérez-Carrasco MJ, Muñoz de Luna J, Vázquez D, Sánchez-Ramos C. Effects of light-emitting diode radiations on human retinal pigment epithelial cells in vitro. Photochem Photobiol. 2013 Mar-Apr;89(2):468-73. http://dx.doi.org/10.1111/j.1751-1097.2012.01237.x. PMid:22989198.

56. Yoshida A, Yoshino F, Makita T, Maehata Y, Higashi K, Miyamoto C, et al. Reactive oxygen species production in mitochondria of human gingival fibroblast induced by blue light irradiation. J Photochem Photobiol B. 2013 Dec;129:1-5. http://dx.doi.org/10.1016/j.jphotobiol.2013.09.003. PMid:24141287.

57. Buravlev EA, Zhidkova TV, Osipov AN, Vladimirov YA. Are the mitochondrial respiratory complexes blocked by NO the targets for the laser and LED therapy? Lasers Med Sci. 2015 Jan;30(1):173-80. http://dx.doi.org/10.1007/s10103-014-1639-8. PMid:25118663.

58. Lev-Tov H, Mamalis A, Brody N, Siegel D, Jagdeo J. Inhibition of fibroblast proliferation *in vitro* using red light-emitting diodes. Dermatol Surg. 2013 Aug;39(8):1167-70. http://dx.doi.org/10.1111/dsu.12212. PMid:23590233.

59. Rimessi A, Giorgi C, Pinton P, Rizzuto R. The versatility of mitochondrial calcium signals: from stimulation of cell metabolism to induction of cell death. Biochim Biophys Acta. 2008 Jul-Aug;1777(7-8):808-16. http://dx.doi.org/10.1016/j.bbabio.2008.05.449. PMid:18573473.

60. Huang L, Wu S, Xing D. High fluence low-power laser irradiation induces apoptosis via inactivation of Akt/GSK3β signaling pathway. J Cell Physiol. 2011 Mar;226(3):588-601. http://dx.doi.org/10.1002/jcp.22367. PMid:20683916.

61. Sun X, Wu S, Xing D. The reactive oxygen species-Src-Stat3 pathway provokes negative feedback inhibition of apoptosis induced by high-fluence low-power laser irradiation. FEBS J. 2010 Nov;277(22):4789-802. http://dx.doi.org/10.1111/j.1742-4658.2010.07884.x. PMid:20977672.

62. Wu S, Xing D, Gao X, Chen WR. High fluence low-power laser irradiation induces mitochondrial permeability transition mediated by reactive oxygen species. J Cell Physiol. 2009 Mar;218(3):603-11. http://dx.doi.org/10.1002/jcp.21636. PMid:19006121.

63. Koutná M, Janisch R, Veselská R. Effects of low-power laser irradiation on cell proliferation. Scr Med (Brno). 2003 Jun;76(3):163-72.

64. Belletti S, Uggeri J, Mergoni G, Vescovi P, Merigo E, Fornaini C, et al. Effects of 915 nm GaAs diode laser on mitochondria of human dermal fibroblasts: analysis with confocal microscopy. Lasers Med Sci. 2015 Jan;30(1):375-81. http://dx.doi.org/10.1007/s10103-014-1651-z. PMid:25351448.

65. Magrini TD, Santos NV, Milazzotto MP, Cerchiaro G, Martinho HS. Low-level laser therapy on MCF-7 cells: a micro-Fourier transform infrared spectroscopy study. J Biomed Opt. 2012 Oct;17(10):101516. http://dx.doi.org/10.1117/1.JBO.17.10.101516. PMid:23223992.

66. Buravlev EA, Zhidkova TV, Vladimirov YA, Osipov AN. Effects of laser and LED radiation on mitochondrial respiration in experimental endotoxic shock. Lasers Med Sci. 2013 May;28(3):785-90. http://dx.doi.org/10.1007/s10103-012-1155-7. PMid:22797824.

67. Karadag A, Yesilyurt A, Unal S, Keskin I, Demirin H, Uras N, et al. A chromosomal-effect study of intensive phototherapy versus conventional phototherapy in newborns with jaundice. Mutat Res. 2009 May;676(1-2):17-20. http://dx.doi.org/10.1016/j.mrgentox.2009.03.008. PMid:19376266.

68. Freitas LF, Hamblin MR. Proposed mechanisms of photobiomodulation or low-level light therapy. IEEE J Sel Top Quantum Electron. 2016 May-Jun;22(3):7000417. http://dx.doi.org/10.1109/JSTQE.2016.2561201. PMid:28070154.

69. International Commission on Non-Ionizing Radiation Protection – ICNIRP. ICNIRP Guidelines on Limits of Exposure to Laser Radiation of Wavelengths between 180 nm and 1,000 µm. Health Phys. 2013 Sep;105(3):271-95. http://dx.doi.org/10.1097/HP.0b013e3182983fd4. PMid:30522251.

70. Marshall J. Radiation and the ageing eye. Ophthalmic Physiol Opt. 1985;5(3):241-63. PMid:3900875.

71. Young RW. Solar radiation and age-related macular degeneration. Surv Ophthalmol. 1988 Jan-Feb;32(4):252-69. http://dx.doi.org/10.1016/0039-6257(88)90174-9. PMid:3279560.

72. Remé CE. The dark side of light: rhodopsin and the silent death of vision the proctor lecture. Invest Ophthalmol Vis Sci. 2005 Aug;46(8):2672-82. http://dx.doi.org/10.1167/iovs.04-1095. PMid:16043837.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

*CORRESPONDING AUTHOR

Ana Claudia Pavarina, UNESP – Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Odontologia de Araraquara, Departamento de Materiais Odontológicos e Prótese, Rua Humaitá, 1680, 14801-385 Araraquara - SP, Brasil, e-mail: ana.pavarina@unesp.br

Received: October 25, 2023
Accepted: October 26, 2023