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Review article

Application of photosensitive dental materials as a novel antimicrobial option in dentistry: A literature review

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Abstract The formation of dental plaque is well-known for its role in causing various oral infections, such as tooth decay, inflammation of the dental pulp, gum disease, and infections of the oral mucosa like peri-implantitis and denture stomatitis. These infections primarily affect the local area of the mouth, but if not treated, they can potentially lead to life-threatening conditions. Traditional methods of mechanical and chemical antimicrobial treatment have limitations in fully eliminating microorganisms and preventing the formation of biofilms. Additionally, these methods can contribute to the development of drug-resistant microorganisms and disrupt the natural balance of oral bacteria. Antimicrobial photodynamic therapy (aPDT) is a technique that utilizes low-power lasers with specific wavelengths in combination with a photosensitizing agent called photosensitizer to kill microorganisms. By inducing damage through reactive oxygen species (ROS), aPDT offers a new approach to addressing dental plaque and associated microbial biofilms, aiming to improve oral health outcomes. Recently, photosensitizers have been incorporated into dental materials to create photosensitive dental materials. This article aimed to review the use of photosensitive dental materials for aPDT as an innovative antimicrobial option in dentistry, with the goal of enhancing oral health.

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Introduction

Dental plaque formation is known to lead to various oral infections, such as white spot lesions, peri-implantitis, and denture stomatitis.[1] Conventional mechanical and chemical antimicrobial methods have limitations in completely eradicating microorganisms and preventing the formation of biofilms. In addition, they have the potential to aid in the emergence of drug-resistant microorganisms and disturb the equilibrium of bacteria in the mouth.[2] Consequently, there is a requirement for targeted approaches that can efficiently eliminate dental plaque, minimize microbial biofilms and bacterial presence, and support sustained oral well-being.

One promising approach to combat microbial infections involves using reactive oxygen species (ROS) as antimicrobial agents.[3] This strategy aims to generate ROS, which can disrupt bacterial growth and replication through various mechanisms like causing DNA damage and interfering with cellular metabolism.[4] Antimicrobial photodynamic therapy (aPDT) is an example of an antimicrobial strategy based on ROS. It is a non-invasive treatment that utilizes safe photosensitizers (PSs). When oxygen is present, the activation of PSs using a visible light source leads to the generation of ROS, which subsequently deactivate microorganisms.[5]

aPDT offers several potential advantages. aPDT is effective regardless of microbial antibiotic resistance. Importantly, it hasn't demonstrated bacteria developing resistance even after 20 cycles of partial killing and regrowth. aPDT can be performed in outpatient or day-case settings, and repeated doses can be given without the need for limitations on the total dose. Another advantage is that resistance to treatment does not develop with repeated sessions.[6,7]

Recently, there has been a growing interest in incorporating PS agents into dental materials.[8—17] This new technique offers several advantages, including reducing patient cooperation, minimizing chair time, and aiming at preventive care. However, it's important to note that the addition of PS agents to dental materials can have negative effects on the physical and mechanical properties of these materials. Based on our knowledge, no study reviews the antimicrobial effect of photosensitive dental materials, as well as their physical and mechanical properties. Therefore, this article aimed to review the use of photosensitive dental materials for aPDT as an innovative antimicrobial option in dentistry, with the goal of enhancing oral health.

Antimicrobial photodynamic therapy

aPDT consists of the three crucial elements: the PS, light with the appropriate wavelength, and oxygen dissolved in the cells.[18] aPDT refers to a photochemical reaction that relies on oxygen and is triggered by light activation of a PS. This reaction generates cytotoxic reactive oxygen species, with singlet oxygen being the predominant one. The mechanism of aPDT can be summarized as follows: the PS is excited and enters a long-lasting excited triplet state. This energy is then transferred to neighboring molecules, typically molecular oxygen, resulting in the formation of highly reactive and cytotoxic ROS like hydroxyl radicals and singlet oxygen.[19,20] These cytotoxic species oxidize cellular components such as plasma membranes and DNA, leading to cell death. aPDT exhibits a high degree of selectivity towards microorganisms or diseased tissues, such as cancer cells. In aPDT, only cells that have accumulated the PS and are exposed to light are eliminated.[7,21] Consequently, aPDT can be repeated multiple sessions without causing cumulative toxicity since it is a non-invasive procedure.[7]

Light source

Light is essential for aPDT as it activates the photosensitizer, leading to the production of reactive oxygen species. Therefore, the light sources employed in aPDT, including commonly utilized options like light amplification by stimulated emission of radiation (lasers) and light emitting diodes (LEDs), are of utmost importance and must meet specific requirements to ensure the effectiveness of the treatment.[22]

One of the light sources utilized in aPDT is the laser. Laser power refers to the amount of energy delivered by a laser beam per unit of time and per unit of area. High-power lasers have an output exceeding 1 kW, whereas low-power lasers have an output equal to or less than 1 kW. Generally, low-power lasers are employed in aPDT.[23] This is because high-power lasers, which are more suitable for surgical purposes, can elevate the temperature within the pulp and around the periodontal ligament, potentially causing bone resorption or pulp necrosis, in addition to being more expensive.[23,24] On the other hand, low-power lasers typically have a power output ranging from 30 to 100 mW, a wavelength between 630 and 904 nm, and minimal thermal effects.[23]

Another light source commonly used in aPDT is LED. LEDs are semiconductor-based devices with two leads that use electricity to stimulate the emission of light through the recombination of electrons and holes in the semiconductor material, without a significant increase in temperature. LEDs can be designed to emit light in different colors of the visible spectrum, including red, blue, and green, as well as in the near-infrared region ($>$700 nm).[7,25] LEDs, despite lacking the monochromatic quality of lasers, can emit strong light across a broad spectrum. While lasers are better at tissue penetration, LEDs are cost-effective, versatile, and can be arranged in different configurations to illuminate large spaces effectively. Their ability to generate light waves of varying lengths and sufficient power makes them advantageous for various applications.[26]

Various factors influence the choice of light source in dental procedures, including cost and access, as well as depth penetration. Here are some key points regarding these factors:

1. Cost and access: Currently, there are low-cost portable light sources available that assist clinicians in directing light to the intended site. LED is one such light source commonly used in dental clinics. LEDs have lower costs compared to lasers and do not require extensive operator training.[6]

2. Depth penetration: The effectiveness of aPDT relies on the light source's ability to penetrate to the desired depth. To achieve a prevention effect and combat microorganisms like *Streptococcus mutans*, a light source with low power or low intensity is typically used. Usually, these light sources function using a power level of 100 mV or less, and they release energy within the range of visible light (wavelengths between 400 and 700 nm). This energy can be emitted either in the ultraviolet range (200—400 nm) or in the near-infrared range (700—1500 nm). In cases where deeper oral infections, such as peri-implantitis, need to be treated, a light source with greater penetration depth is beneficial. Wavelengths between 600 and 800 nm are employed in such situations, as they can penetrate deeply into tissue (5.5—6.5 mm) and enhance the effectiveness of the treatment.[26—29]

Photosensitizer

PSs are substances that can absorb light at a specific wavelength and initiate chemical and physical reactions. When exposed to light of the appropriate wavelength, the PS undergoes a transition from its ground singlet state (^{0}PS) to a singlet excited state (^{1}PS*); then this state (^{1}PS$*$) undergoes inter-system crossing (ISC), transforming into a relatively long-lasting triplet state (^{3}PS$*$).[30] The efficiency of the ISC process and the duration of the triplet state are important characteristics of an effective PS.[31] The triplet state plays a crucial role in generating ROS through two different photochemical processes known as Type-I (electron transfer) and Type-II reactions (energy transfer).[32]

In Type-I reactions, the PS in its excited triplet state interacts with biomolecules, resulting in the production of free radicals and radical ions. These species then react with oxygen, leading to the generation of ROS. In Type-II reactions, the PS in its excited triplet state reacts with molecular oxygen in its ground state, producing highly reactive singlet oxygen that is toxic to cells.[33] Both Type-I and Type-II reactions occur simultaneously, and their balance is influenced by various factors such as the specific PS used, oxygen and substrate concentrations, and the PS's affinity for the substrate. However, it is important to note that singlet oxygen generation, particularly through Type-II reactions, is considered the main mechanism underlying aPDT.[34]

PSs can be categorized as organic (e.g., curcumin and riboflavin) or inorganic (e.g., metal oxide-based). Inorganic PSs have the inherent property of generating electron-hole pairs when exposed to light, leading to a charge-separated state that favors the Type-I pathway. On the other hand, organic PSs are typically involved in Type-II aPDT.[32]

Photosensitizer in dentistry

In the field of dentistry, various PSs have been used; some of the commonly used compounds in dental practices as PSs include curcumin (Cur), riboflavin, and rose bengal. These PSs are classified into different types based on their chemical structures:[26]

1 *Xanthenes compound*: Xanthenes are cyclic compounds consisting of three aromatic rings arranged in a linear fashion with an oxygen atom in the center. These compounds have the ability to absorb light in the visible spectral range. Xanthenes, including rose bengal, are known for their presence in the cytoplasm and their inability to bind to the cell membrane.[26] Rose bengal, a halide derivative of fluorescein, possesses several advantageous properties for its application in aPDT. It exhibits strong antimicrobial properties, is cost-effective, biodegradable, and non-toxic. Moreover, rose bengal contains free amino groups that are conducive to chemical bonding.[35] It is also highly efficient in generating singlet oxygen, making it a suitable choice for aPDT. When employed in aPDT, rose bengal can effectively eliminate microorganisms such as viruses, bacteria, and protozoa.[36] The activation of the type II reaction occurs when rose bengal is exposed to light at a wavelength of 532 nm, resulting in the production of products comprising 80 % singlet oxygen and 20 % superoxide anions.[37]

2 *Phenolic compound*: Polyphenols are a class of molecules that consist of one or more phenolic rings and possess a range of biological activities.[38] These activities include antioxidant, antibacterial, antiviral, and anti-inflammatory properties, which make them potential candidates for the treatment of infections and other diseases.[39] Polyphenolic natural compounds have a long history of being used in drug discovery due to their unique structures, diverse chemical and biological properties, as well as their ability to combat microbial infections and reduce inflammation.[40] Several specific polyphenolic natural compounds, such as Curcumin (Cur), riboflavin, quercetin, and resveratrol, have attracted attention in the field of aPDT.

Cur, which absorbs light in the blue wavelength range of the visible spectrum (300—500 nm),[41] has been found to reduce inflammation and eliminate pathogens in periodontal tissue and its surroundings. Its application in aPDT has been effective in improving periodontal disease severity and overall oral conditions.[26] Resveratrol, a polyphenolic compound found in nature, has a wide range of light absorption from 290 nm to 360 nm.[42] Research has demonstrated that when resveratrol is present at a concentration of 800 μg/mL, it effectively hinders the growth of *S. mutans*, a bacterium linked to tooth decay; additionally, resveratrol has exhibited antimicrobial activity against *Porphyromonas gingivalis*, a bacterium linked to periodontal disease.[43,44]

Riboflavin is an essential vitamin that has been considered as a natural PS for dentistry. It is biocompatible and can induce oxidative damage when exposed to blue light, even with the use of LED devices for curing dental materials. This makes riboflavin an efficient PS for dental applications.[45] Quercetin, on the other hand, is a flavonol and polyphenolic compound found in plants. It possesses antioxidant and anti-inflammatory properties.[46] Quercetin has two absorption bands, with maximum absorption occurring at 380 and 258 nm.[47] When activated by light at 405 ± 10 nm, quercetin exhibits a strong biological effect at micromolar concentrations. Researchers have been particularly interested in the combination of quercetin and blue laser light for the effective degradation of *S. mutans* biofilm in dental caries.[48] This combination could serve as a supplementary strategy to inhibit microbial growth and reduce the risk of drug resistance.[48] Overall, these PSs hold promise for their application in dental photodynamic therapy. Their use may contribute to improved treatment outcomes in dental caries and other oral infections.

3 *Phenothiazines compound*: Phenothiazines such as methylene blue, indocyanine green, and toluidine blue are commonly used as PSs in aPDT. However, their therapeutic effectiveness is limited due to their toxicity.[26] Methylene blue has gained popularity in dentistry because it can absorb light in the red-light region, allowing for deeper tissue penetration. It has low toxicity and effectively kills cariogenic bacteria.[49] Previous studies have shown that methylene blue-mediated aPDT can significantly reduce the presence of *Enterococcus faecalis* and *Staphylococcus aureus*.[20,50] Indocyanine green-mediated aPDT has the advantage of selectively targeting cells and generating high levels of singlet oxygen species, making it a more precise therapy with fewer adverse effects.[20] It has high absorption in the near-infrared range and has been shown to be taken up significantly by periodontal pathogens such as *P. gingivalis* and *Aggregatibacter actinomycetemcomitans*, making it highly effective in eliminating microorganisms associated with periodontitis.[51—53] Indocyanine green-mediated aPDT has also been effective against antimicrobial-resistant strains of common bacterial species.[52] Toluidine blue has been extensively studied for its ability to inactivate pathogenic microorganisms. It absorbs light at a maximum wavelength of 630 nm in the red light spectrum, allowing it to inactivate both gram-positive and gram-negative bacteria.[26] aPDT mediated by toluidine blue has antifungal effects against oral *Candida* spp and antimicrobial effects against *S. mutans*.[54,55] Previous studies have shown that toluidine blue-mediated aPDT can be used as an adjunctive treatment to improve clinical symptoms of periodontal disease, including reducing the depth of periodontal pockets and enhancing clinical attachment levels.[20,56]

4 *Chlorins compound*: Chlorins are compounds with photochemical properties suitable for aPDT. They possess a high quantum yield of singlet oxygen and absorb light at longer wavelengths, which is advantageous for treatment in biological tissues.[26,57] One derivative of chlorin called fotoenticine has emerged as a promising photosensitizer. It has an absorption band ranging from 660 to 680 nm.[58,59] Pervious study investigated the application of fotoenticine in aPDT for the treatment of dental caries.[60] One significant benefit of utilizing fotoenticine is the substantial reduction in the total number of microorganisms, including *streptococci*, *lactobacilli*, and yeasts. They found that fotoenticine-mediated aPDT successfully disrupted biofilm structures. By targeting and disrupting biofilms, fotoenticine-mediated aPDT may help prevent the progression of caries. Furthermore, the treatment with fotoenticine resulted in reduced levels of lactic acid. Lactic acid is produced by bacteria during the fermentation of dietary sugars and contributes to the demineralization of tooth enamel. By lowering lactic acid levels, fotoenticine-mediated aPDT may help mitigate the acid-induced damage to teeth.[20,60]

5 *Metal compound*: Metal nanoparticles, including titanium dioxide (TiO_2) and zinc oxide (ZnO), are considered a new generation of photosensitizers.[61] These nanoparticles possess inherent antimicrobial properties; however, the effectiveness of these properties is dependent on the dosage.[62] Increasing the concentration of nanoparticles enhances their antimicrobial properties, but it may also reduce their biocompatibility due to the inherent toxicity of the metal and the solubility of the nanoparticles, which is determined by the metal's chemical properties, uptake, and its ability to induce oxidative stress.[63,64] On the other hand, applying lower concentrations of these nanoparticles diminishes their antimicrobial properties. To address this issue, a promising approach involves combining these nanoparticles in low concentrations with aPDT, followed by ROS release.[15,65] This combination strategy improves the antimicrobial properties of the nanoparticles while minimizing potential side effects.

Photosensitive dental materials

Until recently, aPDT using PS has primarily been applied to the tooth surface, with studies focusing on its antimicrobial properties in dentistry.[66—68] However, researchers have now started incorporating PSs into various dental materials such as composite, Polymethyl methacrylate (PMMA), and dental implants (Table 1).[8,12,16] This innovation has given rise to the development of photosensitive dental materials, which offer several advantages.

By incorporating PS into dental materials (Fig. 1), a new technique has emerged that allows for targeted antimicrobial treatment. These photosensitive dental materials can be activated using light of specific wavelengths, which activates the PS and leads to the production of reactive oxygen species. This, in turn, causes a selective destruction of bacteria and other microorganisms, promoting antimicrobial effects.

The use of photosensitive dental materials has several benefits. Firstly, it reduces the need for patient cooperation during treatment, as the materials can be activated using light without relying on patient compliance. This is particularly useful in cases where patients may have difficulty maintaining proper oral hygiene or have limited mobility. Secondly, incorporating PS into dental materials minimizes chair time for patients. Traditional antimicrobial treatments, such as the application of antimicrobial agents or antibiotics, often require extended contact time to achieve desired effects. With photosensitive dental materials, the antimicrobial action is activated rapidly upon exposure to light, significantly reducing the time needed for treatment. Lastly, this technique has a preventive care aspect. By incorporating PS into dental materials, such as dental implants or restorative composites, it is possible to provide a continuous antimicrobial effect. This can help

Table 1 Photosensitive dental materials.

Dental material		Photosensitizer			Photodynamic therapy			Microorganism	Pro-inflammatory cytokines	Additional test	Refs
Classification	Type	Classification	Type	Concentration	Light source	Wavelength	Time				
Polymers	Polymethyl methacrylate	Organic	NR	256 μg/mL 512 μg/mL 1024 μg/mL	LED	450 ± 30 nm	1 min	*C. albicans* *S. aureus* *S. sobrinus* *A. naeslundii*	TNF-α IL-1β IL-6	N/D	[8]
Polymers	Polymethyl methacrylate	Organic	*U. lactuca*	0 % (Control) 0.2 % 0.5 % 1 % 2.5 % 5 % 10 %	Blue laser	450 ± 10 nm	N/A	*S. mutans*		FS	[9]
Resin-based composite	Orthodontic composite	Organic-Inorganic	cCur/ZnONPs	0 % 1.5 % 2.5 % 5 % 7.5 % 10 %	LED	435 ± 20 nm	5 min	*S. mutans* *S. sobrinus* *L. acidophilus*	N/D	SBS ARI	[10]
Resin-based composite	Orthodontic composite	Organic	Riboflavin Rose bengal	0 % 0.1 % 0.5 %	UVA	375 nm	30 min	*S. mutans*	N/D	DoF ARI	[11]
Resin-based composite	Restorative composite	Organic	Riboflavin	0 % 0.1 % 0.5 %	UVA	375 nm	30 min	*S. mutans*	N/D	DoF ARI μ-TBS	[12]
Resin-based composite	Composite	Organic	Riboflavin	0.1–10 %	LED (BioLight)	450	1 min	*S. mutans*	N/D	Water sorption Solubility SBS FS	[13]
Resin-based composite	Activa BioActive Base/Liner	Organic	Cur	0 % (Control) 0.5 % 1 % 2 % 5 %	LED	435 ± 20 nm	5 min	*S. mutans*	N/D	N/D	[14]
Metal	Orthodontic miniscrew	Inorganic	ZnO	0.1 g	LED	450 ± 10 nm	1 min	*P. gingivitis* *P. intermedia,* *A.actinomycetemcomitans*	TNF-α IL-1β IL-6	N/D	[15]

Metal	Dental implant	Organic	MB-loaded PLGANPs	50 μg/mL	Diode laser	810 nm	1 min	*P. gingivalis*	N/D	FM FS Surface roughness	[16]
Elastomeric material	Elastomeric ligature	Organic-Inorganic	rGO-nCur	0 % 1.25 % 2.5 % 5 % 7.5 % 10 %	Diode laser	450 ± 10 nm	5 min	*S. mutans*	N/D	TS Force decay Extension to TS	[17]

Abbreviations: ARI, Adhesive remnant index; *A. naeslundii*, *Actinomyces naeslundii*; *A. actinomycetemcomitans, Aggregatibacter actinomycetemcomitans; C. albicans*, *Candida albicans*; NR, nano-resveratrol; Cur, curcumin; cCur/ZnONPs, cationic curcumin doped zinc oxide nanoparticles; DoF, Degree of Conversion; FS. Flexural strength; FM, Flexural modulus; g, gram; μg/mL, microgram per milliliter; rGO-nCur, reduced Graphene oxide-nano curcumin; IL, Interleukin; LED, Light-emitting diode; Nm, Nanometer; N/A, Not applicable; , N/D, Not done; Min, Minute; MB-loaded PLGA NPs, methylene blue-loaded poly (D,L-lactide-co-glycolide) nanoparticles; μ-TBS, Micro-tensile bond strength; *P. gingivitis*, *Porphyromonas gingivitis*; *P. intermedia*, *Prevotella intermedia*; *S. sanguinis*, *Streptococcus sanguinis*; *S. mutans*, *Streptococcus mutans*; *S. aureus*, *Staphylococcus aureus*; *S. sobrinus*, *Streptococcus sobrinus*; SBS, Shear bond strength; Refs, References; TS, Tensile strength; TNF-α, Tumor necrosis factor-α; UVA, Ultraviolet light source A; *U. lactuca, Ulva lactuca*; ZnO, Zinc oxide.

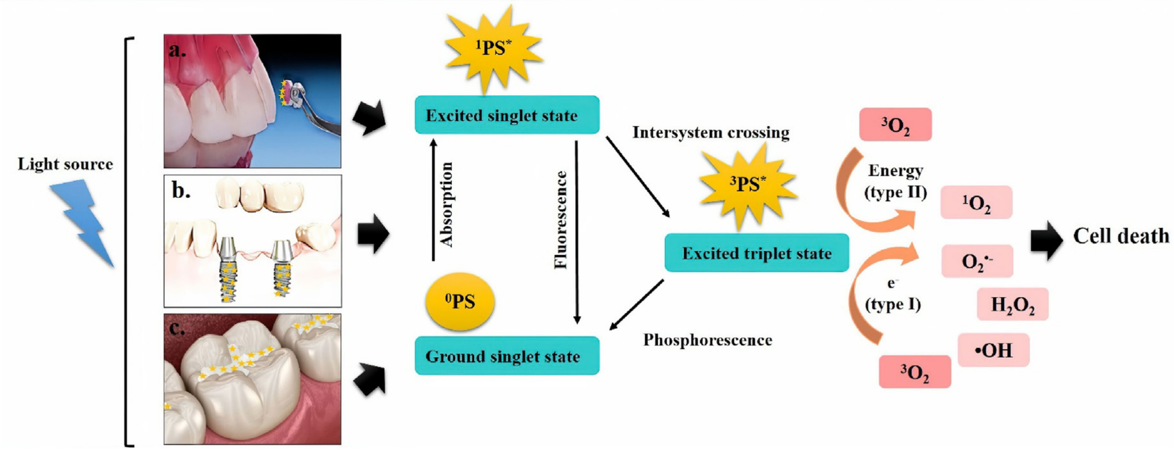

Figure 1 The antimicrobial mechanism of photodynamic therapy using photosensitive dental materials; a. Photosensitive orthodontic composite, b. Photosensitive dental implant/miniscrew, and c. Photosensitive restorative composite. PS: photosensitizer, ^{0}PS: Ground singlet state, ^{1}PS*: Excited singlet state,^{3}PS*: Excited triplet state.

prevent the development of biofilms or secondary infections, promoting long-term oral health.

Antimicrobial properties

White spot lesions, dental caries, and periodontal complication are common oral infection that caused by dental plaque. *S. mutans* is a type of coccus bacteria that is Gram-positive and encapsulated. It plays a crucial role in causing tooth decay.[69] Tooth decay happens when the population of *S. mutans* bacteria reaches 50 % of the total bacterial population.[70] *S. mutans* produces a sticky substance called extracellular polysaccharides (EPS) that helps them stick to tooth enamel and form a biofilm. Once they attach to the tooth surface, they generate acids that destroy the hard tissues of the tooth.[71] Several studies have shown that dental materials containing PSs like *Ulva lactuca*, cationic Cur doped ZnO nanoparticles (cCur/ZnONPs), Cur, riboflavin, rose bengal, and reduced graphene oxide-nano Cur (rGO-nCur) can reduce the number of *S. mutans* colonies when used in aPDT.[9—12,14,17] The effectiveness of these materials in reducing *S. mutans* colonies depends on the concentration of the PS. Furthermore, research by Pourhajiagher et al. demonstrated a significant decrease in the number of *S. mutans* colonies in the biofilm over a period of 60 days.[14] Another study showed that, during the first 60 days, the bacteria did not grow in the culture medium. After that, although some bacteria were found in the culture medium, their numbers were lower than the control group. Up to the 150th day, the number of colonies that grew was significantly less than the control group; however at the 180th day, there was no significant difference compared to the control group.[10]

One of the common complications related to periodontal health is peri-implantitis, a condition that can ultimately lead to the failure of dental implants or orthodontic miniscrews. This condition is caused by the accumulation of anaerobic biofilms, including *P. gingivitis*, *Prevotella intermedia*, and *A. actinomycetemcomitans*. These biofilms trigger an immune response, resulting in the activation and migration of immune cells such as neutrophils and macrophages to the surrounding tissues of the implant.[72] Once the macrophages are activated, they release pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Clinically, these changes manifest as signs of inflammation around the dental implant or orthodontic miniscrew, including bleeding on probing, increased pocket depth, and loss of bone tissue.[73] Bahrami et al. conducted a study showing that photosensitive orthodontic miniscrews coated with ZnONPs reduced the presence of periodontal pathogens (*P. gingivitis, P. intermedia*, and *A. actinomycetemcomitans*) when subjected to aPDT (LED, 450 nm, 1 min).[15] These findings are consistent with the study conducted by Aldegheishem et al., where dental implants were coated with methylene blue-loaded poly (D,L-lactide-co-glycolide) nanoparticles (MB-loaded PLGANPs) and aPDT (diode laser, 810 nm, 1 min) was performed. This study demonstrated a significant reduction in the viability of *P. gingivalis* compared to a control group.[16]

Another common complication in periodontal health is denture stomatitis. Pourhajibagher et al. introduced a light-sensitive acrylic material and examined the efficacy of aPDT on complex biofilms formed by multiple microorganisms including *Candida albicans*, *S. aureus*, *S.sobrinus*, and *Actinomyces naeslundii*. They incorporated nano-resveratrol (NR) into the acrylic resin and investigated its impact. The findings of their study demonstrated that aPDT mediated by NR significantly decreased the abundance of polymicrobial biofilms compared to a control group consisting of acrylic discs lacking NR and treated with phosphate-buffered saline. The reduction in biofilm presence was observed to be influenced by the dosage of NR utilized.[8]

Physico-mechanical properties

In order to maintain the physical and mechanical properties of dental materials, it is important to consider the addition of PS carefully. Several studies have investigated the effects of incorporating different PS into dental materials and have observed an indirect relationship between PS concentration and material strength.

For instance, Pourhajibagher et al. conducted a study where they added *U. lactuca* to PMMA to create a photosensitive acrylic resin. They found that increasing concentrations of *U. lactuca* led to a decrease in flexural strength (FS). However, the significant difference in FS was only observed in groups containing 2.5 %, 5 %, and 10 % of *U. lactuca* compared to the control group. They recommended adding *U. lactuca* at a concentration of 1 % to PMMA, as it increased the material's antibacterial and anti-biofilm activities without adversely affecting FS.[9] Similarly, another study focused on modifying composite resin with cCur/ZnONPs. This modification was found to reduce the shear bond strength (SBS), but the highest concentration of cCur/ZnONPs (7.5 %) still provided an acceptable SBS value. This modified composite resin could potentially serve as an orthodontic adhesive additive to control cariogenic multispecies biofilm and reduce their metabolic activity.[10] In a study by Hashem, riboflavin was added to restorative composite resin at concentrations of 0.1 % and 0.5 %. The baseline micro-tensile bond strength (μ-TBS) showed no statistically significant difference between the groups. However, after 30 days, the μ-TBS scores for the 0.1 % riboflavin group were significantly higher compared to the 0.5 % riboflavin group.[12]

This observed relationship between PS concentration and material strength has been noted in other articles as well.[14] While increasing PS concentration can enhance the antimicrobial properties of dental materials, it can have a negative impact on their mechanical properties. This could be due to PS acting as an impurity and interfering with the polymerization process. Studies by Alqerban and Hashem demonstrated that adding PS to orthodontic and restorative composites decreased the degree of conversion, which is crucial for governing the physical and mechanical properties of adhesive resins.[11,12] Possible explanations for this phenomenon include the agglomeration of the PS used, such as rose bengal or riboflavin, which could impede the curing process.[12,74] Nonetheless, Alqerban concluded that a modified composite resin with 0.1 % of either Rose Bengal or riboflavin after aPDT could be used for bonding orthodontic brackets with substantial antibacterial properties.[11] Additionally, Comeau et al. found that adding up to 1.5 % riboflavin had minimal impact on the flexural strength FS or SBS of resin composites, while effectively reducing water sorption and solubility.[13]

Other studies have explored the effects of PS on different dental materials. Ghanemi et al. investigated the use of elastomeric ligatures coated with 5 % rGO-nCur and found that they did not adversely affect the physical and mechanical characteristics of the ligatures, such as tensile strength, extension to tensile strength, and force decay. These coated ligatures could be employed to inhibit the formation of *S. mutans* biofilms around orthodontic brackets.[17] Additionally, Aldegheishem et al. examined the mechanical properties (such as flexural modulus, FS, and surface roughness) of dental implants coated with MB-loaded PLGANPs at a concentration of 50 μg/mL. They found that the mechanical properties and surface integrity of the dental implants were not compromised by the coating.[16]

From a clinical perspective, it is crucial to thoroughly research and carefully select the optimal modifications for dental materials, taking into account their overall properties. Future studies should focus on determining the ideal concentration of PS and developing standardized protocols for aPDT in dental applications.

Inflammatory response

One potential side effect of ROS-mediated strategies, such as aPDT, is the induction of inflammation through the generation of ROS and activation of the nuclear factor-κB (NF-κB) signaling pathway.[75,76] However, it is important to recognize that the effect of PDT on inflammation can vary depending on various factors, including the type and concentration of photosensitizer agents, the radiation protocol, and the specific cellular and tissue environment.[8,15]

Fortunately, there are some studies that have shown promising results in terms of reducing inflammation with the use of aPDT. For example, a study conducted on human gingival fibroblast (HGF) cells demonstrated that an acrylic resin containing resveratrol as a photosensitizer resulted in decreased gene expression of inflammatory cytokines and did not induce an inflammatory response.[8] Additionally, Bahrami et al. conducted an *in vitro* study to evaluate the impact of aPDT mediated by ZnONPs on gene expression of inflammatory cytokines from HGF around coated miniscrews with ZnONPs.[15] The results of their study demonstrated that aPDT mediated with ZnONPs successfully reduced the expression of inflammatory cytokines including TNF-α, IL-1β, and IL-6 in the HGF cells around the coated miniscrews. However, since the PSs used in these studies had anti-inflammatory properties, and according to the available evidence, aPDT mediated by these PSs has been shown to decrease the gene expression of inflammatory cytokines, further research is necessary to fully explore this potential and generate more substantial evidence in the future.

In conclusion, the incorporation of photosensitizers into dental materials has given rise to the development of photosensitive dental materials, offering several advantages in terms of antimicrobial treatment, patient cooperation, chair time reduction, and preventive care. Further research and development in this field hold promise for improving dental treatments and enhancing overall oral health.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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