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Review article

Boosting the antibacterial potency of antimicrobial photodynamic therapy against oral pathogens through supplement agents: A narrative review

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Abstract Antimicrobial photodynamic therapy (aPDT) is a promising approach for managing oral infections; however, it faces several limitations, such as limited penetration depth, biofilm resistance, and photosensitizer dimerization or aggregation. To address these challenges, the current study reviews new techniques to enhance the antibacterial effectiveness of aPDT. Recent advances have pointed out the potential of novel supplement agents—including inorganic salts, antimicrobial peptides, surfactant media, and postbiotics—to overcome these limitations significantly. Inorganic salts like potassium iodide, potassium selenocyanate, and potassium thiocyanate can enhance aPDT by generating additional reactive species or increasing reactive oxygen species (ROS)-mediated cytotoxicity. Antimicrobial peptides disrupt membranes selectively and help penetrate deeper into biofilms, while surfactant media improve the solubility of photosensitizers and prevent their aggregation, thereby maximizing ROS production. Postbiotics not only lead to improved biofilm penetration but also cause increased oxidative stress on microbial cells. Therefore, these combined strategies have

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markedly improved microbial eradication, particularly against resilient biofilms and antibiotic-resistant strains. Although integrating these innovative supplement agents signals a new era for photodynamic therapy in oral healthcare—presenting renewed opportunities for practical, non-invasive, and resistance-free infection control—further studies are necessary to validate these findings, establish standardized protocols, and evaluate the long-term safety and clinical benefits of these combined strategies.

Introduction

The oral cavity harbors a diverse microbiota pivotal in maintaining oral health. While most of these microorganisms exist in a state of symbiosis with the host, various predisposing factors—such as poor oral hygiene, systemic illnesses, or immunosuppression—can disrupt this microbial balance, leading to pathogenic shifts in the oral microflora.[1] Such dysbiosis may manifest as common oral infections, including periodontal disease, dental caries, and infections associated with *Candida* biofilms.[2] Various mechanical and chemical antimicrobial strategies are employed to manage and prevent these conditions, including routine tooth brushing, chlorhexidine mouthwashes, fluoride rinses, and topical fluoride applications. Although these methods are generally effective, they are associated with several limitations, including the requirement for consistent patient cooperation, the potential for undesirable side effects (e.g., tooth discoloration, taste alterations), and the growing concern of microbial resistance.[3]

Antimicrobial photodynamic therapy (aPDT) emerges as a promising adjunctive or alternative approach to conventional methods. It is a non-invasive and topical treatment modality that operates through the interplay of three core components: a photosensitizer (PS), light of a specific wavelength, and molecular oxygen.[4,5] Upon irradiation with light (Fig. 1), the PS transitions from its ground singlet state (^{1}PS) to an excited singlet state (^{1}PS*) and subsequently to a more stable triplet excited state (^{3}PS$*$) via intersystem crossing. This triplet state enables the PS to engage in two primary types of photochemical reactions: Type I (electron transfer) and Type II (energy transfer). These reactions facilitate the generation of reactive oxygen species (ROS), such as hydroxyl radicals (HO•) and singlet oxygen ($^1O_2$), which in turn oxidize lipids, proteins, and nucleic acids—culminating in microbial cell death.[6,7]

aPDT offers the advantage of minimizing systemic toxicity and can be repeatedly administered without cumulative dose limitations. However, its clinical efficacy can be hindered by factors such as microbial resistance and the limited ability of PSs to penetrate complex microbial biofilms.[8] To overcome these limitations, several combinatorial strategies have been proposed. These include: (1) co-administration with antibiotics to enhance antimicrobial efficacy,[9] (2) incorporation of antimicrobial peptides (e.g., Aurein, Polymyxin B, Magainin) to facilitate cellular penetration,[10] (3) use of antimicrobial nanoparticles such as silver and zinc oxide,[11] (4) integration with non-toxic inorganic salts (e.g., sodium azide, potassium iodide, potassium bromide, potassium selenocyanate, sodium nitrite, and potassium thiocyanate), which can participate in ROS-generating reactions,[8] (5) supplementation with vitamins such as riboflavin (vitamin B2) and vitamin D, which may enhance ROS production and oxidative stress within microbial cells,[12] (6) combining with postbiotics, defined as inanimate microorganisms and the metabolic and secretory products generated by microbes during growth and fermentation, which can inhibit the growth and colonization of microorganisms through the production of antimicrobial peptides, organic acids, and hydrogen peroxide,[13,14] and (7) integrating with surfactant media (such as sodium dodecyl sulfate) to prevent dimerization or aggregation of the PS.[15]

Among these strategies, applying inorganic salts, antimicrobial peptides, surfactant media, and postbiotics—as novel supplement agents—remains relatively underexplored. Emerging studies suggest that these agents may significantly potentiate the antimicrobial efficacy of aPDT against oral pathogens. To address these challenges, the current study reviewed new techniques to enhance the antibacterial effectiveness of aPDT.

New supplement agents

aPDT, a promising alternative to conventional antimicrobial strategies, has several limitations, including limited penetration depth, biofilm resistance, and dimerization or aggregation of the PS. First, the light used in a PDT, particularly in the visible spectrum, has limited tissue penetration, making it less effective for deep-seated infections or biofilms in areas with poor light accessibility.[16] Second, aPDT can be effective against biofilms, but thick or mature biofilms can still pose a challenge due to limited PS penetration and light absorption/scattering within the biofilm matrix; also, aPDT alone is effective against many pathogens, its effectiveness can be limited, especially against gram-negative bacteria.[4] Finally, dimerization or aggregation of the PS also affects the antibacterial efficacy of aPDT.[15]

Recent articles highlighted the potential of new supplement agents, including inorganic salts, antimicrobial peptides, surfactant media, and postbiotics, to significantly enhance microbial killing by aPDT (refer to Table 1).

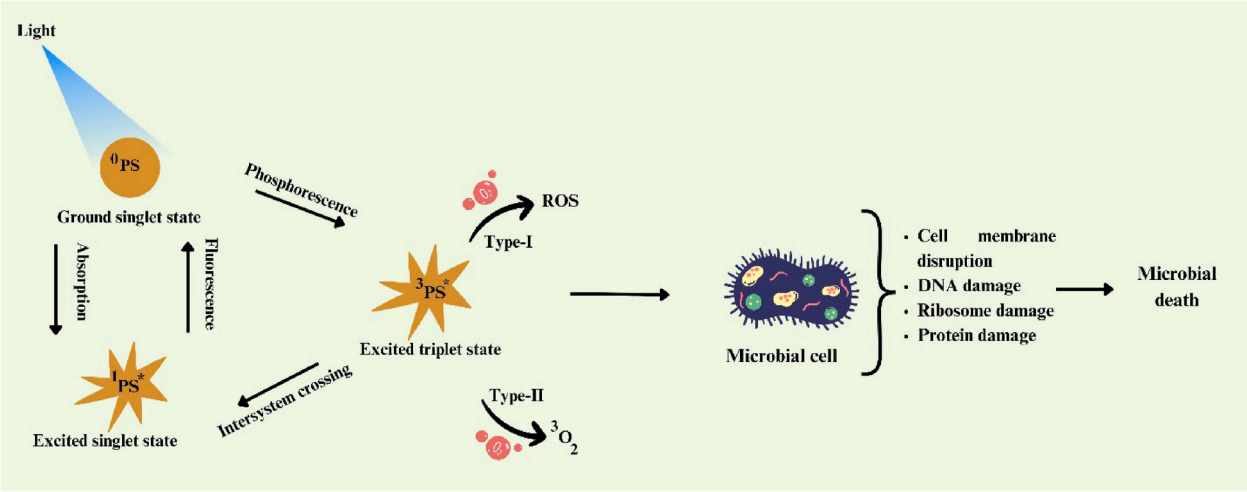

Figure 1 The mechanism of antimicrobial photodynamic therapy and its potentially effect on microbial cells. PS: photosensitizer, ^{0}PS: Ground singlet state, ^{1}PS*: Excited singlet state, ^{3}PS*: Excited triplet state.

Inorganic salts

Inorganic salts are biocompatible and safe supplement agents that can enhance the antimicrobial properties of aPDT. We discussed how different types of inorganic salts improve the antimicrobial effectiveness of aPDT against oral pathogens:

1. *Iodide*: Potassium iodide, a non-toxic inorganic salt, may enhance the effectiveness of aPDT. In a study by Damrongrungruang et al., researchers evaluated various concentrations of bisdemethoxycurcumin (20, 40, and 80 μM) combined with potassium iodide (100 mM) during aPDT using a dental LED (450 nm, 95 J/cm^2, 950 mW/cm^2, for 95 s) against *Candida albicans*. The results indicated that a concentration of 40 μM bisdemethoxycurcumin, in conjunction with 100 mM potassium iodide and the dental LED, significantly reduced *C. albicans* biofilms after 6 h, demonstrating effectiveness comparable to that of nystatin.[21] Additionally, Wen et al. found that adding potassium iodide (100 mM), a non-toxic salt, enhanced the efficacy of Rose Bengal when activated by green light (540 nm, 100 mW/cm^2).[28] This led to a remarkable increase in bacterial killing—up to 6 logs—against the fungal yeast *C. albicans*, Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa*, as well as the Gram-positive bacterium methicillin-resistant *Staphylococcus aureus*.[28] These findings were consistent with those of Huang et al., who examined the synergistic effect of combining titanium dioxide nanoparticles (TiO_2NP)-mediated aPDT (LED, 365 nm, 16 mW/cm^2) with potassium iodide (at concentrations of 1 or 10 mM). Their study showed this combination effectively reduced the colony count of methicillin-resistant *S. aureus*, *E. coli*, and *C. albicans* by 6 logs.[31] Huang et al. attributed this synergistic effect to the generation of microbicidal molecular iodine (I_2/I_3^-).[29]

In another study by Yuana et al., the antimicrobial properties of aPDT were investigated in combination with potassium iodide on human gingival fibroblast (HGF) cells. Their findings revealed that potassium iodide not only enhanced methylene blue aPDT against *Enterococcus faecalis* in both planktonic and biofilm states, even in hypoxic conditions, but also produced a long-lasting bactericidal effect after the illumination ended;[24] these results were due to the generation of hydrogen peroxide and free iodine, with iodine radicals potentially formed under hypoxia. Ultimately, they showed that methylene blue (0.4 μM for planktonic and 10 μM for biofilm)-mediated aPDT (LED, 660 nm, 50 mW/cm^2) plus potassium iodide (100 mM) dramatically increased the sterilization effect against *E. faecalis*, while safeguarding HGF cells.[24] Shih et al. assessed the efficacy of potassium iodide in combination with temoporfin-mediated aPDT against oral pathogens under hypoxic or normoxic conditions.[22] The results indicated this combination reduced the minimum inhibitory concentrations and minimum bactericidal concentrations of *Lactobacillus acidophilus* and *Lactobacillus paracasei* under both normoxic and hypoxic conditions due to increased hydrogen peroxide production. Temoporfin enhanced the removal of biofilms of *Aggregatibacter actinomycetemcomitans*, *E. faecalis*, and *S. aureus* under normoxic conditions, while also reducing the expression of antibiotic resistance-related genes in methicillin-resistant *S. aureus*. Furthermore, the combination of temoporfin with ampicillin or chlorhexidine significantly enhanced the bactericidal effect on methicillin-resistant *S. aureus*, providing a potential clinical application of temoporfin in combating oral pathogens and preventing oral diseases.[22] Based on prior studies, the recommended concentration of potassium iodide for combination with aPDT is 100 mM. At lower concentrations (up to 10 mM), iodine radicals primarily contribute to antimicrobial activity. However, when the concentration of potassium iodide increases to 100 mM or higher (up to 400 mM), free iodine becomes the main agent responsible for the antimicrobial effect.[8,29,32]

2. *Bromide*: Sodium bromide, which is a close analog of potassium iodide, has been shown to enhance titanium dioxide (TiO_2)-mediated aPDT (360 nm, 16 mW/cm^2, 1 J/

Table 1 Summary of findings from articles evaluating the impact of combining supplement agents with antimicrobial photodynamic therapy on oral pathogens.

Study design	Microorganism	Culture type	Photosensitizer	Light dose	Wave length	Pre-irradiation time	Irradiation time	Supplement agent	Outcomes	Refs
In vitro	*Streptococcus mutans*	Planktonic Biofilm	Riboflavin	60–80 J/cm^2	450 nm	5 min	1 min	Postbiotic (*Lactobacillus* species)	Postbiotics enhanced the effectiveness of riboflavin-mediated aPDT against *S. mutans* in both biofilm and planktonic phases.	14
Randomized clinical trial	Endodontic bacteria (patients)	–	Methylene blue	30 J/cm^2	660 nm	1 min	3 min	Surfactant (0.25 % Sodium dodecyl sulfate)	Combination of aPDT-based methylene blue by Sodium dodecyl sulfate improved root canal disinfection.	17
Randomized clinical trial	Periodontal pathogens (patients)	–	Methylene blue	30 J/cm^2	660 nm	1 min	2 min	Surfactant (0.25 % Sodium dodecyl sulfate)	Adjuvant aPDT improved periodontal treatment outcomes.	18
In vitro	Multi-species periodontal biofilm: *Streptococcus oralis* *Fusobacterium nucleatum* *Porphyromonas gingivalis* *Aggregatibacter actinomycetemcomitans*	Biofilm	Chlorin-e6 (Ce6)	60 J/cm^2	450 nm	5 min	1 min	Antimicrobial peptide (LL-37)	LL-37 improved Ce6-mediated killing and ROS production.	19
In vitro	*Streptococcus mutans*	Biofilm	Hypericin	18 J/cm^2	590 nm	10 min	3 min	Antimicrobial peptide (Dermcidin-1L [DCD-1L])	DCD-1L improved antibacterial efficacy of hypericin-mediated aPDT against *S. mutans*.	20
In vitro	*Candida albicans*	Biofilm	Bisdemeth oxycurcumin	90 J/cm^2	450 nm	20 min	95 s	Inorganic salt (Potassium iodide)	Potassium iodide synergistically enhanced bisdemethoxycurcumin-mediated aPDT against *C. albicans*.	21
In vitro	*A. actinomy cetemcomitans* *Lactobacillus acidophilus* *Enterococcus faecalis* *S. mutans* *Staphylococcus aureus* methicillin-resistant *S. aureus*	Planktonic	Temoporfin	10 J/cm^2	652 nm	5 min	5 min	Inorganic salt (Potassium iodide)	Potassium iodide boosted Temoporfin-mediated aPDT, including under hypoxia.	22
In vitro	*E. faecalis*	Biofilm	Emodin	30 J/cm^2	660 nm	Immediate	5 min	Antimicrobial peptide (DCD-1L)	DCD-1L improved efficacy of emodin-mediated aPDT against	23

(*continued on next page*)

Table 1 (*continued*)

Study design	Microorganism	Culture type	Photosensitizer	Light dose	Wave length	Pre-irradiation time	Irradiation time	Supplement agent	Outcomes	Refs
									E. faecalis.	
In vitro	*A. actinomycetemcomitans* *P. gingivalis*	Biofilm	Methylene blue	30 J/cm^2	660 nm	Immediate	1–5 min	Surfactant (0.25 % Sodium dodecyl sulfate)	Sodium dodecyl sulfate stabilized methylene blue and improved microbial killing.	15
In vitro	*E. faecalis*	Biofilm	Methylene blue	10 J/cm^2	660 nm	Immediate	1 min	Inorganic salt (Potassium iodide)	Potassium iodide increased efficacy of methylene blue-mediated aPDT to kill *E. faecalis* biofilms.	24
In vitro	*E. faecalis*	Biofilm	Methylene blue Ce6	30 J/cm^2	660 nm	10 min	5 min	Antimicrobial peptide (Aurein 1.2)	Aurein 1.2 as an antimicrobial peptide enhanced reactive oxygen species production and biofilm destruction.	25
In vitro	*E. faecalis*	Biofilm	Methylene blue Rose bengal	10 J/cm^2	660 nm 540 nm	30 min	10 min	Inorganic salt (Selenocyanate)	$SeCN^-$ potentiated killing against *E. faecalis* biofilms.	26
In vitro	*E. faecalis*	Biofilm	Methylene blue Curcumin Ce6	30 J/cm^2	660 nm 450 nm 660 nm	10 min	5 min	Antimicrobial peptide (Aurein 1.2)	Aurein 1.2 improved photosensitizer delivery and biofilm eradication.	27
In vitro *In vivo*	*C. albicans*	Biofilm	Rose bengal	18 J/cm^2	540 nm	15 min	180 s	Inorganic salt (Potassium iodide)	Potassium iodide enhanced rose bengal-mediated photoinactivation of *C. albicans*.	28
In vitro	*C. albicans*	Biofilm	Photofrin	2 J/cm^2	630 nm	15 min	60 s	Inorganic salt (Potassium iodide)	Potassium iodide potentiated photofrin-mediated killing of *Candida* biofilms.	29
In vitro	*C. albicans*	Planktonic	Titanium dioxide nanoparticles	1 J/cm^2	360 nm	Immediate	1 min	Inorganic salt (Sodium bromide)	Bromide increased titanium dioxide photocatalysis against *C. albicans*.	30
In vitro	*C. albicans*	Planktonic	Titanium dioxide nanoparticles	1 J/cm^2	365 nm	Immediate	1 min	Inorganic salt (Potassium iodide)	Potassium iodide significantly enhanced titanium dioxide-mediated *Candida* killing.	31

Abbreviation: aPDT, Antimicrobial photodynamic therapy; Min, Minute; nm, Nanometer; Refs, References; s, Second; J/cm^2, Joule per square centimeter.

cm^2, 1 min) at concentrations ranging from 0 to 10 mM.[30] This combination resulted in an impressive increase in the killing efficacy against methicillin-resistant *S. aureus*, *E. coli*, and *C. albicans* by up to 3 logs.[30] This enhancement likely stems from the oxidation of bromide, a two-electron oxidation to hypobromite (one of the oxidized bromine species), which occurs due to direct oxidation by photoactivated TiO_2, rather than by an intermediate oxygen-containing oxidizing species.[30,32] However, Hamblin et al. found that sodium bromide did not demonstrate any potentiation of bacterial or fungal killing when combined with other PSs like Rose Bengal and methylene blue.[32] Conversely, incorporating potassium iodide with these PSs resulted in significant enhancements in the killing of both Gram-positive and Gram-negative microorganisms.[32] According to findings by Wu et al., the optimal concentration of sodium bromide varies according to the type of microorganism.[30] For instance, a concentration of 1.5 mM bromide was sufficient to achieve an additional 2–3 logs of killing against methicillin-resistant *S. aureus*, while 10 mM bromide achieved an impressive 4 logs of extra killing against both *E. coli* and *C. albicans*.[30] Consequently, further research is warranted to determine the most effective concentration of sodium bromide, especially in conjunction with various PSs.

3. *Selenocyanate*: Selenocyanate has been proposed as a low-toxicity inorganic selenium species suitable for dietary supplementation.[33] Huang et al. reported that potassium selenocyanate, at concentrations of up to 100 mM, can significantly enhance aPDI mediated by various PSs, including methylene blue, Rose Bengal, and 5,10,15,20-tetrakis (4-sulfonatophenyl) porphyrin dihydrochloride, with effective concentrations as low as 200 nM. When a mixture of selenocyanate and these PSs was illuminated before the addition of bacteria, there was a remarkable reduction of up to 6 logs in the bacterial count, with Gram-negative bacteria (like *E. coli*) being more affected than Gram-positive bacteria (such as methicillin-resistant *S. aureus* and *E. faecalis)*.[26] However, it was observed that the antibacterial activity diminished rapidly, decreasing significantly within 20 min. They demonstrated this antibacterial activity may result from the formation of selenocyanogen $(SeCN)_2$ through its reaction with singlet oxygen ($^1O_2$). This is indicated by the quenching of $^1O_2$ by $SeCN^-$ and the increased photoconsumption of oxygen.[26]
4. *Azide*: Azide, particularly sodium azide (NaN_3), has also been explored for its potential to potentiate aPDT. Sodium azide, a known quencher of singlet oxygen, paradoxically enhances bacterial killing when combined with certain phenothiazinium dyes, such as methylene blue, under photoactivation.[8] Hamblin et al. demonstrated that sodium azide, although traditionally considered a singlet oxygen scavenger, undergoes electron transfer reactions when interacting with excited PSs, producing azidyl radicals ($N_3\bullet$) that are highly reactive and capable of microbial cell destruction. Unlike other salts, azide does not generate long-lived reactive species like molecular iodine or peroxides, and its potentiation effect is highly dependent on the type of PS and irradiation conditions.[8] Despite its strong potentiating effects *in vitro*, the toxicity of sodium azide to human cells limits its clinical application, making it less favorable compared to salts like potassium iodide.
5. *Nitrite*: Nitrite (NO_2^-), typically in the form of sodium nitrite, has been shown to enhance aPDT through mechanisms involving the generation of peroxynitrite ($ONOO^-$) and reactive nitrogen species (RNS). Under photoactivation, nitrite can react with singlet oxygen or other reactive intermediates to form powerful oxidants such as peroxynitrite, contributing to microbial killing. Studies have demonstrated that sodium nitrite can significantly boost the photoinactivation of both Gram-positive and Gram-negative bacteria when used alongside various PSs.[8] Furthermore, nitrite-induced nitration of tyrosine residues within microbial proteins (resulting in nitrotyrosine formation) adds an antimicrobial mechanism. The safety profile of nitrite at low concentrations and its ability to generate RNS support its potential as an effective supplement agent in aPDT, particularly for oral disinfection purposes.[8]
6. *Thiocyanate*: Thiocyanate (SCN^-), available as potassium thiocyanate, also demonstrates synergistic effects when used with aPDT.[34] The enhancement mechanism involves a dual Type I and Type II photochemical process, initially producing sulfite ions that subsequently form highly reactive sulfur trioxide radical anions ($SO_3\bullet^-$).[34] These radicals can damage bacterial membranes, proteins, and DNA, leading to efficient microbial killing. Hamblin et al.[8] demonstrated that thiocyanate-based potentiation is distinct from iodide or selenocyanate, offering an alternative pathway for augmenting microbial destruction. The advantage of thiocyanate lies in its relatively low toxicity and the feasibility of integrating it into clinical protocols, especially in treating oral biofilm-associated infections.[8,35]

Antimicrobial peptides

In recent years, antimicrobial peptides have emerged as potent adjuncts to aPDT against oral pathogens. Peptides such as LL-37 and dermcidin-1 L (DCD-1 L) exhibit broad-spectrum antimicrobial activity by disrupting microbial membranes and inhibiting biofilm formation.[19,23] Gabriel Garcia de Carvalho et al. developed a nanoemulsion system incorporating chlorin-e6 conjugated to LL-37, demonstrating a significant reduction in the viability of multi-species biofilms associated with periodontitis during aPDT.[19] The conjugation enhanced ROS production and improved PS delivery and retention within the biofilm matrix.[19] Similarly, Pourhajibagher et al. introduced aptamer-decorated emodin nanoparticles coupled with DCD-1L, achieving targeted delivery and enhanced photodynamic antimicrobial activity against *E. faecalis* biofilms.[23] Their findings revealed significant biofilm destruction and down-regulation of virulence genes, emphasizing the synergistic potential of combining antimicrobial peptides with aPDT.[23] These studies underline the promising role of antimicrobial peptides as supplement agents, particularly in targeting biofilms and overcoming microbial resistance mechanisms within the oral cavity.

Surfactant media

Surfactants, especially sodium dodecyl sulfate (SDS), have been employed to optimize the efficacy of aPDT by preventing PS aggregation. Aggregation reduces the availability of monomeric PS molecules, thereby diminishing ROS generation and antimicrobial effects.[15,18] Tortamano et al. demonstrated that methylene blue dissolved in a surfactant vehicle such as SDS exhibited superior photodynamic inactivation of periodontal pathogens compared to aqueous solutions alone.[15] The surfactant medium stabilized the PS in its monomeric form, enhanced light absorption, and improved penetration into biofilms.[15] Similarly, Kassa et al. applied a methylene blue-surfactant formulation as an adjunctive therapy in periodontal treatment, reporting significant reductions in bacterial load and improved clinical outcomes.[18] Therefore, using surfactants represents an effective strategy to maximize PS efficiency, ensuring higher ROS production and better bacterial eradication during aPDT procedures.

Postbiotics

Postbiotics are inanimate microbial cells and the metabolic products they produce during growth and fermentation. These bioactive compounds, which include antimicrobial peptides, organic acids, and hydrogen peroxide, can inhibit the growth and colonization of harmful microorganisms. This offers a new approach to enhance the antibacterial effects of aPDT by improving biofilm penetration and increasing oxidative stress on microbial cells, leading to more effective microbial destruction. Additionally, postbiotics have been shown to work synergistically with PSs used in aPDT by boosting the production of ROS and destabilizing biofilms, which often resist conventional therapies.[13,14] For example, research by Pourhajibagher et al. demonstrated that metabolites derived from *Lactobacillus* species can enhance the effectiveness of riboflavin-mediated aPDT against *S. mutans*, a key bacterium involved in dental caries.[14] By combining aPDT with postbiotic compounds, researchers aim to address limitations such as poor biofilm penetration and microbial resistance, providing a more potent and targeted treatment for oral infections.[13,14] However, since this field is relatively new, further research is needed to optimize protocols, evaluate long-term safety, and standardize the application of postbiotics in clinical aPDT strategies.

Potential clinical applications

Integrating inorganic salts, antimicrobial peptides, surfactant media, and postbiotics into aPDT protocols holds considerable promise for clinical applications in dentistry and oral healthcare. Enhanced aPDT regimens have demonstrated significant potential in managing periodontitis, peri-implantitis, endodontic infections, and oral candidiasis.[15,18,19,23,32] In periodontal therapy, adjunctive use of methylene blue with surfactants and potassium iodide has shown improved biofilm disruption and clinical attachment gains.[15,18] In endodontics, combining aPDT with potassium iodide or antimicrobial peptides like DCD-1L has improved the disinfection of infected root canals, even in hypoxic conditions.[17,23] Additionally, treatments targeting *Candida* biofilms on oral mucosa have achieved substantial success by combining bisdemethoxycurcumin, potassium iodide, and blue LED irradiation.[21] Research indicates that combining potassium iodide, Lactobacillus species (as a postbiotic), and DCD-1L with aPDT exhibits antibacterial effects against *S. mutans*, the primary microorganism responsible for tooth decay.[14,20,22] Beyond dentistry, the principles established here may extend to treating mucosal infections, wound infections, and potentially systemic fungal infections by localized photodynamic approaches. Further clinical trials are needed to develop optimal protocols, safety profiles, and standardized guidelines for these enhanced therapies.

Conclusion

Research on the effects of aPDT-based supplement agents on oral pathogens is still in its early stages, but the findings thus far have been encouraging. Due to the limited number of articles available, establishing a specific protocol has not been possible. Among the supplement agents examined—such as inorganic salts, antimicrobial peptides, surfactant media, and postbiotics—potassium iodide has garnered significant attention as a non-toxic inorganic salt, particularly at a concentration of 100 mM. However, there is a strong consensus on the necessity for further studies to determine the optimal protocol, including concentration, duration of use, and the best combinations with each type of photosensitizer. Additionally, evaluating these combined strategies' long-term safety and clinical benefits is essential. Future studies, which can be divided into laboratory and clinical studies, hold the potential to improve dental treatments significantly. In laboratory studies, researchers can combine aPDT-based supplement agents with dental materials and appliances and evaluate basic tests (microbial and molecular tests such as antimicrobial effects, biocompatibility against human cells, and inflammatory gene expression) and dentistry tests (like impact on physico-mechanical properties of dental materials). In clinical studies, researchers can use these enhancer combinations tailored to specific oral diseases or the current status and results of relevant clinical trials, offering a positive outlook for the future of dental treatments.

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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