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REVIEW ON PHOTOSENSITIZER POTENTIAL OF NATURAL DYES FOR ANTIMICROBIALS USING PHOTODYNAMIC INACTIVATION

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ABSTRACT

Infectious diseases still threaten human life, with incidents continuing to increase every year. The increase in antibiotic resistance in recent years has been one of the causes. This incident triggered research to find alternative antibacterial therapies. One such alternative therapy is Photodynamic Inactivation (PDI). This paper reviews the application of PDI for treating diseases caused by microorganisms, especially dermatitis, periodontitis, blood transfusions, and foodborne diseases, emphasizing the use of natural dyes as photosensitizers. The source for this article was obtained from several indexed databases, such as the National Center for Biotechnology Information (NCBI), Elsevier, and Google Scholar, from 2002 to 2024. The keywords used included “photodynamic therapy", “photodynamic inactivation (PDI)”, "antimicrobial photodynamic therapy (aPDT)", “laser-activated disinfection”, “photoactive disinfection”, “LED”, “natural photosensitizer”, “curcumin”, “riboflavin”, “hypericin”, “chlorophyll and chlorophyllin. Original (clinical and experimental) studies, case series, case reports, and reviews were also included. Letters to the editor and commentaries are excluded. After reviewing 148 relevant articles, 57 were selected. Full texts were read, and data were extracted and entered into tables. The review demonstrated that natural photosensitizers, such as curcumin, hypericin, riboflavin, and chlorophyll derivatives, have the potential to reduce the number of microorganisms in PDI therapy. Photosensitizers can be obtained from several natural sources. Using the PDI procedure, the ROS produced have been proven to effectively inhibit pathogenic microorganisms and can be widely used to treat diseases caused by microorganisms.

Keywords: *curcumin, hypericin, riboflavin, chlorophyllin derivatives, PDI, natural dye, antimicrobial.*

INTRODUCTION

Antimicrobial resistance (AMR) is an important issue. The data in 2019 estimated that AMR, particularly bacteria, was directly responsible for 1.27 million deaths worldwide and contributed to 4.95 million mortalities (Murray et al., 2022). The increasing incidence of AMR requires a new approach to address the problem. PDI is a novel antimicrobial therapeutic technique that has shown effectiveness in deactivating a broad spectrum of microorganisms, including those that are resistant to traditional antimicrobials.

PDI involves interaction between photosensitizer (PS) and light in an aerobic environment. This interaction produces reactive oxygen species (ROS) that can destroy microorganisms rapidly (Henderson & Dougherty, 1992; Pucelik & Dąbrowski, 2022). PS is a light-sensitive compound that acts as a medicinal compound in this system.

PDI is an evolution of photodynamic therapy (PDT) that was previously used to treat cancer. Anticancer PDT is based on the use of PS, which selectively accumulates in malignant tissues. PS is then exposed to light at a specific wavelength that corresponds to the absorption maximum of the photosensitizer, leading to cell death (Agostinis et al., 2011; Dolmans et al., 2003; Dougherty et al., 1998).

PDT and PDI involve three main components: photosensitizers, light, and oxygen. Notably, none of these compounds were toxic. However, when they interact, a photochemical reaction is initiated, which ultimately produces ROS, especially singlet oxygen ($^1O_2$), as the main product (Henderson & Dougherty, 1992).

This review focuses on the natural application of photosensitizers in antimicrobials using PDI procedures. Natural dyes, such as curcumin, hypericin, riboflavin, and chlorophyll derivatives, have been explored. A limited number of studies directly discuss this topic. Therefore, this study aimed to examine the potential of natural dyes as photosensitizers in PDI for diseases caused by microbes.

RESEARCH METHOD

Tools and Materials

The source for this article was obtained from several indexed databases such as the National Center for Biotechnology Information (NCBI), Elsevier, and Google Scholar from 2002 to 2024 in the form of published articles in PDF.

Article Selection Criteria

Articles that met the inclusion criteria were organized with the assistance of a Mendeley reference manager.

Research Procedure

All articles downloaded from the National Center for Biotechnology Information (NCBI), Elsevier, and Google Scholar were imported into the Mendeley reference manager based on specific keywords. Each keyword folder was sorted by searching for keywords that matched the inclusion criteria. Articles that met the exclusion criteria were excluded, resulting in 148 articles that met the inclusion criteria. After evaluating 90 relevant articles, 57 were selected for full-text reading, extraction, and placement in a table.

RESULTS AND DISCUSSION

Photodynamic Therapy (PDT) for Cancer Treatment

PDT is a minimally invasive method used clinically for human oncological diseases, such as breast (Kim et al., 2020), head and neck (Jerjes et al., 2022; van Doeveren et al., 2018), lung (Allison et al., 2011; Allison & Bansal, 2022), prostate (Osuchowski et al., 2021), and skin cancer (Chi et al., 2020).

PDT employs a photosensitizer, which is excited by light at a specific wavelength and subsequently reacts with oxygen molecules to produce ROS in the target tissue, leading to cell death. Compared with routine therapies, photosensitizers require better selectivity toward tumor cells. Once the photosensitizer was concentrated in the tumor lesion, appropriate light irradiation was applied to the lesion (**Figure 1**).

The PDT mechanism for ROS production starts with the absorption of light by the PS. This incident causes the photosensitizer to transform from the ground state (singlet state, ^{1}PS) to the energized singlet state (^{1}PS*). This unstable PS could return to the ground state while releasing fluorescence or heat (internal conversion). ^{1}PS* can also undergo intersystem crossing into an excited triplet state (^{3}PS*) via spin conversion. ^{3}PS* will return to a ground state over phosphorescence or perform two other reactions. The first reaction

occurs when $^{3}PS^{*}$ transfers its energy directly to oxygen (O_2) to produce singlet oxygen ($^{1}O_2$). This reaction is known as a type-II reaction. Other reactions can occur if $^{3}PS^{*}$ reacts straightforwardly with a substrate, such as a membrane or a molecule cell, to produce free radicals or radical ions, which then interact with oxygen to produce ROS, such as H_2O_2, HO•, and $O_2^{-\bullet}$ (Correia et al., 2021). These reactive species can cause oxidative damage that can lead to cell damage (**Figure 1**).

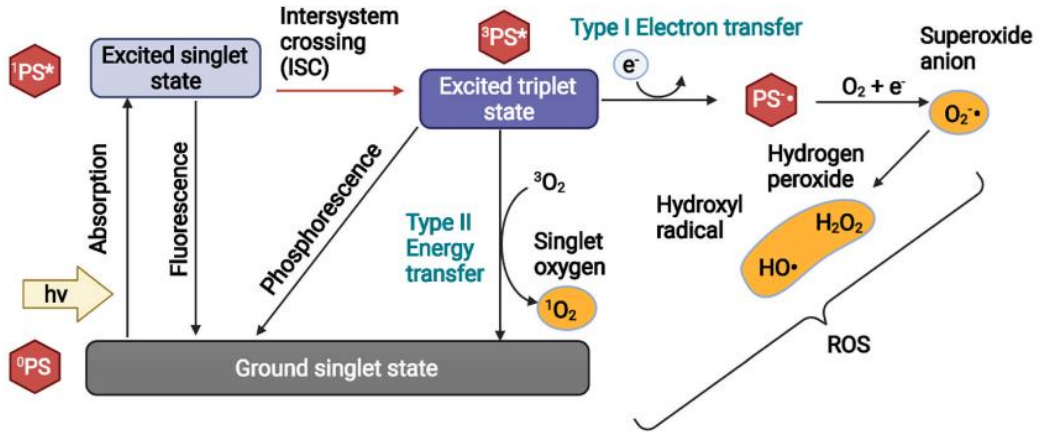

Figure 1. Modified PDT Jablonski diagram based on (Sheng et al., 2022)

PDT is clinically approved for targeting malignant cells, such as tumors and cancers. This minimally invasive approach is clinically advantageous owing to its minimal pain, fewer complications, and faster patient recovery. PDT can initiate tumor cell death both directly and indirectly. The primary mechanism involves the direct destruction of tumor cells by ROS through the induction of apoptosis and necrosis (Li et al., 2020; Hamblin, 2020; Allison and Moghissi, 2013). Additionally, PDT can cause damage to the blood vessels within tumor cells, disrupting the supply of oxygen and nutrients and leading to indirect cell death due to hypoxia (Michael R. Hamblin, 2017; Correia et al., 2021). Finally, PDT can trigger an inflammatory response that activates the immune response in tumor cells (Huang et al., 2018; Correia et al., 2021) (**Figure 2**).

PDI for antimicrobials

PDT has also been used to treat non-oncologic diseases (Correia et al., 2021). This treatment includes acne (Boen et al., 2017), photoaging (Shin et al., 2015), warts (Stender et al., 2012), psoriasis (Makuch et al., 2022), hirsutism (Comacchi et al., 2012), vascular malformations (Jerjes et al., 2011), keloid (Tosa & Ogawa, 2020), and alopecia areata (Garcia-Lara et al., 2020); cardiovascular conditions: esophageal varices (Li et al., 2009) and atherosclerosis (Mytych et al., 2024); neurologic conditions: Alzheimer's disease (Xu et al., 2022); dental conditions: oral lichen planus (Cosgarea et al., 2020); ophthalmologic conditions: central serous chorioretinopathy (Dijk & Boon, 2018) and corneal diseases (Verteporfirina & Verteporfin, 2016); gastrointestinal conditions: Crohn's disease (Espeland et al., 2023); and skeletal conditions: rheumatoid arthritis (Dong et al., 2021). An expansion of the PDT method encompasses the inactivation of viruses and microorganisms, including bacteria, yeasts, and fungi, and is known as PDI (Svyatchenko et al., 2021).

The antimicrobial value of polydispersity index (PDI) has been investigated in various studies since the 1990s. Many of these studies have shown prospective results, often attaining inactivation levels of more than 5 log10 colony forming units (CFU) (Pérez-Laguna et al., 2021). However, it is worth noting that most of this research has been conducted using planktonic cultures. Microorganisms in the form of biofilms are known to show 1000 times greater tolerance to antimicrobial therapy. The biofilm (extracellular polymeric) matrix can protect bacteria by inhibiting PS penetration and restraining light entrance into more

profound layers (Pérez-Laguna et al., 2021). Further research can prove PDI's ability of PDI to inhibit biofilm formation (Warrier et al., 2021). Therefore, treatment problems caused by resistance to antibiotics and antiviral drugs can be overcome using PDI therapy strategies.

PDI can be applied to several areas, including agro-food, human and veterinary pharmaceuticals, biosafety, and wastewater. Many advantages, which ultimately make it very popular, are that PDI is heat-free, fast, and eco-friendly. Moreover, the rapid development of light emitting diodes (LED's) and other light sources makes this procedure inexpensive and simple to maintain (Paskeviciute et al., 2018).

1.1. PDI for Skin Diseases

Approximately 3,000 skin diseases are caused by microorganisms, such as fungi, bacteria, viruses, or allergens (Nigat et al., 2023). Skin infections can easily affect areas with lesions due to burns, trauma, surgery, and coagulopathy (Barra et al., 2015; Dąbrowski et al., 2016).

PDI has the potential to manage diverse cutaneous infections, including fungal, bacterial, and viral infections, and to promote wound healing. Particularly, in chronic wounds, it can combat mixed infections and resistant strains (Gil-Pallares et al., 2024). Considering the ease of using PDI lamps on the skin, mucocutaneous infections are the most common treatment for PDI (Dai et al., 2009). Furthermore, the favorable effects of PDI on host tissues, such as immune response enhancement and growth factor stimulation, may promote enhanced wound healing, supporting its use in the treatment of chronic ulcers (Cieplik et al., 2018; Vallejo et al., 2021).

An important aspect to consider for PDI in skin disease treatment is light penetration into tissues. Penetration is influenced by optical absorption and scattering due to endogenous tissue chromophores, including hemoglobin (absorption <600 nm) and other molecules, such as collagen, NADH, and the lipopigment melanin (400–750 nm, most significant). Therefore, a person's phototype, based on the melanin level, is crucial for estimating the penetration of light into the skin (Gil-Pallares et al., 2024).

In contrast to viruses, for which the therapeutic method is indirect, PDI has a direct impact on the treatment of fungi and bacteria (Vilas Boas et al., 2017). PDI exploits the reliance of the virus on infected host cells. Two hypotheses explain the PDI mechanism in this context. First, infected cells experience accelerated metabolism and capture more PS than healthy cells do, leading to PS accumulation. Upon exposure to light, host cells die. The fatality of host cells inhibits the virus from continuing to replicate, thus stopping the disease chain. Second, in herpes simplex viruses, PS binds to glycoproteins on the virus surface. This binding inhibits virions from exiting the host cell (Vilas Boas et al., 2017).

PDI has been recommended as a therapy for warts and condylomas caused by human papillomavirus (Shen et al., 2022; Fehr et al., 2002). Additionally, PDI using methylene blue has demonstrated efficacy in herpes viruses. Moreover, methylene blue and hypericum extracts have been shown to inactivate adenoviruses, coxsackieviruses, polyomaviruses, and coronaviruses (Praena et al., 2022).

PDI has been proposed for the treatment of ulcers and infected wounds. Bacterial infections inhibit wound healing by prolonging the inflammatory phase and producing virulence factors, such as enterotoxins, matrix metalloproteinases, hyaluronidases, and hemolysins. These factors increase local tissue damage and overwhelm host defense mechanisms (Sun et al., 2020). A previous study showed that PDI reduces bacteria in wounds and accelerates healing (Kawczyk-Krupka et al., 2018; Nesi-Reis et al., 2018; Pérez-Laguna et al., 2021; Sun et al., 2020).

PDI has been used to treat cutaneous fungal infections. Dermatophytes, *Candida spp.*, and *Malassezia spp.* are the principal causative agents of cutaneous fungal infections (Khodadadi et al. 2021). Dermatophytosis is the most common fungal disease worldwide. PDI employs a different method of action than antifungal medicines, which are the main targets of ergosterol synthesis. Furthermore, PDI has been studied for the

treatment of *Candida spp*.-associated stomatitis (Mima et al., 2012) and parasite-induced cutaneous illnesses, such as leishmaniasis (Bogdan, 2020).

1.2. PDI in the Food Sector

Foodborne diseases are mostly caused by foodborne pathogens, which include bacteria, parasites, and viruses. According to data, Shiga toxin-producing *Escherichia coli* (STEC, 6%), *Salmonella* (30%), and norovirus (38%), were the main causes of outbreaks in the United States from 2009 to 2015 (Mattia & Manikonda, 2018). The food industry is also concerned about the rise in pathogenic bacteria that are resistant to antibiotics and other drugs as well as fungi that are resistant to fungicides. Antibiotic-resistant genes and bacteria such as *Salmonella*, *Listeria monocytogenes*, and *Aeromonas hydrophila* have been found in fish and fish products (Sheng & Wang, 2021).

Microbial contamination can occur in fruit and vegetable juices through various means, such as the use of contaminated raw materials for harvesting or washing water in processing machines. The addition of benzoic acid, citric acid, ascorbic acid (Olaniran et al., 2020), or heat treatment (Rawson & Dunlosky, 2011) is often used to reduce the growth of microorganisms and increase their shelf life. However, these methods can cause changes and reductions in the bioactive content of fruit juices (Aghajanzadeh et al., 2023; Rawson & Dunlosky, 2011)

Endogenous and exogenous photosensitizers can be used to control foodborne diseases. Endogenous photosensitizers can reduce pathogens, fungi, and bacterial spoilage in food. However, it is important to note that the exposure time in these studies was a few hours or even days, particularly for ready-to-eat foods (Sheng et al., 2022). Endogenous photosensitizers have low inactivation rates; therefore, exogenous photosensitizers must be added. The key characteristics of exogenous photosensitizers applied to food include PS leaving no hazardous residues, having little impact on the food's organoleptic attributes (visual appearance, flavor, and taste), having no effect on nutritional value, and having low cost.

Curcumin is the most frequently used exogenous photosensitizer in food applications (Cossu et al., 2021). Data indicate that 56% of studies employed curcumin as an exogenous photosensitizer (Sheng et al., 2022). Most curcumin is dissolved in ethanol and diluted for application in fruits (e.g., strawberries, apples, dates, cherries, grapes, and melons), vegetables (e.g., cucumbers, tomatoes, bell peppers, grains, spinach, labyrinth, lettuce, and green beans), animal products (e.g., pork, cheese, beef, chicken, and cooked sausages), and aquaculture products (e.g., RTE salted jellyfish, oysters, and sturgeon).

The concentration of PS, food matrix, target microorganisms, and duration of exposure all affect the efficiency of PDI in decontaminating food. Longer illumination times and higher photosensitizer concentrations often result in the increased antibacterial efficacy of PDI. The effectiveness of PS delivery techniques (such as the application pattern and incubation period) might also affect PDI. There are several different application methods, including immersion, aerosolizations, spraying, coating, and packaging (Oliveira et al., 2018). The physical and chemical characteristics of PS (such as solubility, color, amphipathic, stability, and reactivity), light characteristics (such as wavelength, fluence, and irradiance), and food matrix properties (such as opacity, turbidity, density, organic load, and oxygen concentration) have been mentioned as additional influencing factors (Cossu et al., 2021).

Most food-related studies have found no negative effects of PDI on food quality (**Table I**). The most commonly reported positive effect of PDI on food quality is an increase in shelf life. Other advantages of PDI for food quality include maintaining the quality criteria, preserving sensory attributes, and reducing microbiological deterioration.

1.3. PDI for Blood Transfusion

PDI is frequently used in blood transfusion procedures, such as the Mirasol PRT (Pathogen Reduction Technologies) device. This device deactivates white blood cells and reduces infections in specific blood products. This procedure treats platelets and plasma using UV light and riboflavin in a storage bag. A storage bag is an adaptation of a container used to gather and store platelet products constructed from biocompatible materials. The riboflavin sterile solution (500 µmol/L) was mixed with the blood component at a final concentration of approximately 50 µmol/L. The 0.9% NaCl solution was adjusted with HCl to a pH range of 4.0-5.0. The three mechanisms operate together to reduce the infectivity of pathogens while using the Mirasol PRT architecture. Direct degradation of nucleic acids is the primary mechanism of action (Reddy et al., 2008).

Gram-positive and gram-negative bacteria, as well as enveloped and nonenveloped viruses, have all been examined in relation to pathogen inactivation using the Mirasol PRT approach (Goodrich et al., 2004). These results demonstrate the method's broad suitability and potential for reducing pathogens in blood components (Fast et al., 2006; Cardo et al., 2006; Rentas et al., 2007; Li et al., 2005).

1.4. PDI for Dental and Oral Diseases

The use of PDI in dentistry is becoming increasingly popular, especially for periodontal and mucosal diseases. Bacteria in plaque biofilms cause periodontitis, an inflammatory disease that damages the tissue surrounding the teeth. Gum tissue pockets, attachment loss, bone deterioration, and tooth loss are caused by infection. It impacts the hard and soft tissues of the periodontium (Saini et al., 2009; Böcher et al., 2019).

The microorganisms responsible for the disease include Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia (Torrungruang et al., 2015). Research on the effectiveness of PDI in treating periodontal disease is limited, with no standardization of clinical parameters, such as light dose and PS concentration (Alwaeli et al., 2015; Carvalho et al., 2015). PDI was capable of entirely eliminating the bacterial burden in the planktonic phase and drastically reducing it in biofilm form. PDI was able to completely eliminate the bacterial load in the planktonic phase and significantly reduce it in biofilm form. These findings demonstrated the effectiveness of PDI against metronidazole-resistant periodontal bacteria.

PDI against dental plaque bacteria resistant to metronidazole was assessed by another researcher. According to their research, PDI may reduce biofilm samples and the total microbial burden during the planktonic phase. The photosensitizers employed in PDI applications can penetrate biofilms, as evidenced by confocal fluorescence microscopy. The effectiveness of antimicrobial photodynamic therapy against metronidazole-resistant dental plaque bacteria was clarified in this study. Methylene blue, chlorin-e6, and curcumin, three PDI photosensitizers, were used, and the microbial load and biofilm reduction were encouraging. PDI against dental plaque bacteria resistant to metronidazole was assessed by another researcher. According to their research, PDI may reduce biofilm samples and total microbial burden during the planktonic phase. Confocal fluorescence microscopy research has shown that the photosensitizers utilized in PDI applications can reduce biofilm formation (Zago et al., 2020).

PDI is noninvasive, requires a short treatment time, reduces the likelihood of bacteremia after periodontal debridement, reduces systemic antibiotic administration and the risk of resistance that may arise, and eliminates pathogens in hard-to-reach areas because the photosensitizer is inside the periodontal pocket and can flow over the entire root surface (Park et al., 2020).

Natural photosensitizers for PDI

Photosensitizers are key components of PDI. Numerous studies have developed exogenous photosensitizers by searching for cheaper and nontoxic materials made from natural substances.

Numerous bacteria and fungi possess endogenous PS, including nicotinamide adenine dinucleotide (NADH), flavins, cytochromes, and porphyrins (Wang et al., 2021). Enhancing growth media using δ-aminolevulinic acid (ALA), a naturally occurring heme precursor, can enhance endogenous photosensitizers such as porphyrins (Ghate et al., 2019).

Another study showed that endogenous *P. gingivalis* and *P. intermedia* can produce ROS using PDI techniques (Nielsen et al., 2015a). These two species are black-pigmented bacteroides with endogenous chromophores, including μ-oxo, bisheme, and hematin. In control trials with the riboflavin photosensitizer, μ-oxo, bisheme, and thymethin were likely to act as photosensitizers and inhibit bacterial growth.

Although PDI can be performed with endogenous photosensitizers, the limitations of the results obtained have led most studies to focus on the application of exogenous photosensitizers. Plant pigments, especially pigments that have an absorption spectrum in the Soret area, have the potential to be explored. These natural dyes usually do not have significant side effects compared with synthetic drugs. Several natural photosensitizers, such as curcumin, hypericin, riboflavin, and chlorophyll derivatives, have been studied (**Table I**). Natural photosensitizers have several advantages, particularly for food-related applications, including low toxicity, shorter treatment periods than endogenous PS, broad-spectrum antimicrobial effects, and long-lasting efficacy.

A. Curcumin

Curcumin is a yellow pigment extracted from Curcuma longa and has been used as a spice since ancient times (Rao & Khanum, 2016). Curcumin can absorb blue light (400–500 nm) and can act as a natural PS (**Figure 2**). Curcumin (E100) is classified as a food additive. No cases of toxicity due to the use of curcumin in food have been reported.

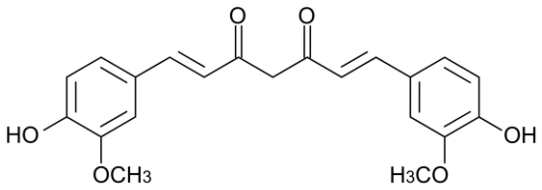

Figure 2. Chemical structure of curcumin

The efficiency of curcumin as a PS has been extensively studied, particularly in its application in the fields of food and periodontal disease. Curcumin can penetrate the interior of the biofilm and inactivate metronidazole resistant bacteria from subgingival plaque (Zago et al., 2020). Its application in periodontal disease can be enhanced by formulating curcumin into graphene quantum dot nanoparticles, which can inhibit Perio-pathogen mixed biofilms (*Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis,* and *Prevotella intermedia*) (Pourhajibagher et al., 2019).

In the food sector, curcumin mediated PDI has been observed to combat contamination in food, including *Staphylococcus epidermidis* and *Escherichia coli* (Bhavya & Hebbar, 2019) as well as filamentous fungi such as *Penicillium chrysogenum*, *Aspergillus flavus* (Al-Asmari et al., 2017), and *Penicillium expansum* (Song et al., 2020). A recent study found that PDI caused the formation of ROS, resulting in oxidative damage and disruption of *Penicillium expansum*'s cellular structure. Furthermore, excessive ROS triggers the antioxidant defense system of the spores.

Curcumin mediated PDI had no negative impact on food quality. It prevented browning and weight loss in Fresh-cut apples and inhibited the activity of enzymes related to food quality, polyphenol oxidase, and peroxidase. Additionally, the treated

apples showed minimal unfavorable changes in total phenolic content, ascorbic acid content, and antioxidant activity (Tao et al., 2019). PDI using curcumin has been proven to increase the shelf life of oysters, sturgeons, and jellyfish (Liu et al., 2016; Gong et al., 2020; Hu et al., 2019).

B. Hypericin

The pigment known as Hypericin (**Figure 3**) is present in a number of species within the genus Hypericum, including basidiomycetes (*Dermocybe* spp.), endophytic fungi (*Thielavia subthermophila*), and *Hypericum perforatum* L. (St. John's wort). Visible light at 585 nm can activate hypericin, and its application in cancer therapy has been well documented. According to popular belief, this pigment is "one of the most potent photosensitizers in nature." Notably, hypericin is neither genotoxic nor toxic (Kairyte et al., 2012; Kubin et al., 2005).

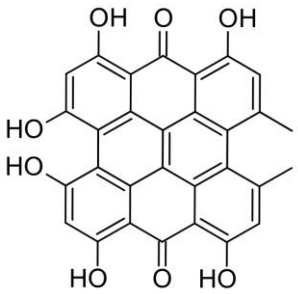

Figure 3. Chemical structure of hypericin

An earlier study found that hypericin-based photosensitization was efficient against food pathogens (Zivile, 2021). The efficacy of hypericin-mediated photodynamics was heavily influenced by cellular shape and PS uptake. Hypericin, with a negative charge, binds to cellular membranes owing to its high lipophilicity (Kubin et al., 2005; Kairyte et al., 2012). The PS effectively killed Gram-positive methicillin-sensitive and resistant *S. aureus* cells (>6 log decrease), but not Gram-negative *E. coli* cells (<0.2 log reduction). This distinction was induced by differing cell wall/membrane architectures that directly altered the cellular uptake of hypericin (Yow et al., 2012).

The fluorescence emission spectra of cell-associated hypericin showed that it binds to both Gram-positive and Gram-negative bacteria quickly and does not require extended incubation periods. Studies have shown that *S. aureus* and its biofilms, as well as *E. faecalis*, *E. coli*, and *P. aeruginosa*, can be effectively eradicated (Kashef et al., 2017; García et al., 2015). Furthermore, hypericin-based photosensitization is effective against microfungi and yeasts in vitro (Aponiene et al., 2015; Paz-Cristobal et al., 2014). However, inactivation of Gram-positive pathogens (*L. monocytogenes*) is more successful than Gram-negative pathogens (*S. enterica*) (Kairyte et al., 2012).

C. Riboflavin

Riboflavin, also known as vitamin B2 (**Figure 4**), is a vitamin found in food products and is utilized as a dietary supplement. Exposure to blue light or light-emitting diodes (LED) induces oxidative damage to riboflavin (Nielsen et al., 2015b). According to research conducted by Nielsen and colleagues, photodynamic therapy (PDT) using blue light and riboflavin as the photosensitizer effectively reduces the number of bacteria involved in periodontal infections, including *P. gingivalis* and *P. intermedia* (Nielsen et al., 2015a) Consequently, further in vitro and clinical studies are needed to afford more precise information regarding the utility and effectiveness of riboflavin as a photosensitizer in periodontitis treatment. Additionally, Kingsley et al., (2018) found that PDT utilizing 0.1% riboflavin and LED 405 nm can reduce Tulane virus on blueberries by 0.51 log PFU/ml after 30 minutes of light exposure. Riboflavin has also been shown to reduce *A. Baumannii* viability (Bustamante and Palavecino, 2023).

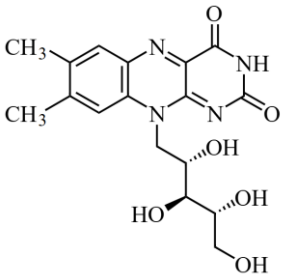

Figure 4. Chemical structure of riboflavin

The formation of ROS in PDI using riboflavin has been proven by several researchers (Khan et al., 2019; Banerjee et al., 2020). Prominent oxidative stress was evaluated using lipid peroxidation as a biomarker when riboflavin was used in photodynamic therapy. Changes in cellular antioxidant levels, decreased lactate dehydrogenase (LDH) activity, and lipid peroxidation have confirmed significant damage to macromolecules, indicating extensive ROS production in bacterial cells (Khan et al., 2019).

The combination of antimicrobial treatment with PDI has also been carried out by several researchers Najari et al., (2024) The study shows that the combination of PDI (riboflavin) and antibiotics (colistin) can improve bacterial reduction. This method has potential implications in the treatment of difficult-to-treat *P. aeruginosa infections. In addition,* an in vivo study of 37 patients using riboflavin-tryptophan gel showed a clinical improvement in acne vulgaris. This noninvasive procedure is useful for the treatment of mild to moderate acne, reducing pore size, and improving skin texture (Wangsuwan and Meephansan, 2019).

D. Chlorophyll Derivatives

Chlorophyll, recognized as a sensitizer for antimicrobial photodynamic therapy (PDI), is a natural substance that is suitable for this purpose (Abrahamse & Hamblin, 2016). Chlorophyll and its derivatives, such as chlorophyllin and chlorin e6, exhibit significant photosensitizing properties (**Figure 5**).

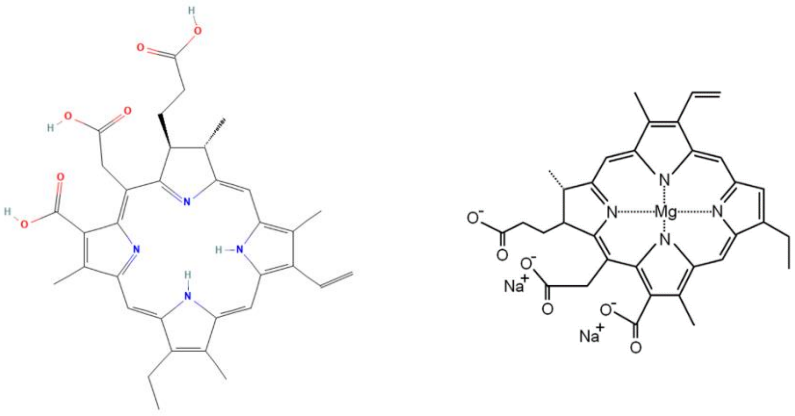

Figure 5. Chemical structure of chlorin e6 (left) and chlorophyllin (right)

Natural chlorin derivatives offer several advantages. These compounds are primarily sourced from plants and algae containing chlorophyll a and b, making them readily available and cost-effective. Extraction methods for these pigments are relatively simple and do not entail significant labor costs. Semi-synthetic chlorophyll compounds such as chlorin e6 have been shown to possess significant bactericidal activity against middle ear disease (Otitis media/OM) pathogens, including Streptococcus pneumoniae, Moraxella catarrhalis, and non-typeable Haemophilus influenzae, which are prevalent in children with OM (Luke-Marshall et al., 2020). Ce6-mediated photodynamic therapy (PDT) effectively mitigates inflammation

induced by acne bacteria and suppresses the expression of proinflammatory cytokines and iNOS in P. acnes (Jeon et al., 2015).

Tabel I. Application of natural dye as Photosensitizer in PDI

Photosensitizer	Target microorganism	Matrixes associated	Light	Results			References
				Control	PDI	Unit	
Curcumin							
Curcumin 60 µM	*P. gingivalis, F. Nucleatum*	Periodontal	LED blue light 440-480 nm, 570 mW/cm^2, 3 min	PS-/L+: 20, 70 PS+/L-: 63, 50	0; 5	%survival	(Mahdi et al., 2015)
Curcumin 5 g/ml	*A. actinomycetemcomitans*	Periodontal	LED blue light 420-480 nm, 400 mW/cm^2, 5 min	PS-/L+: 8.10 PS+/L-: 6.89	5.56	log CFU/mL	(Najafi et al., 2016)
Curcumin and curcuminoid 5 g/L	mixed: *S. mutans* and *L. Acidophilus*	Periodontal	LED 450 nm, 19 mW/cm^2 and 47.5 mW/cm^2	PS+/L-: 100	30.6 (19) 29.6 (47.5)	%survival	(Araújo et al., 2017)
Curcuma longa extract 0.78 µg/ml	*A. actinomycetemcomitans*	Periodontal	LED blue light 420-480 nm, 280 mW/cm^2, 1 min	PS-/L+: 7.42 PS+/L-: 6.81	0	log CFU/mL	(Saitawee et al., 2018)
Graphene quantum dots (GQD)-curcumin 100 µg/ml	perio-pathogen mix biofilms: *A. actinomycetemcomitans* *P. gingivalis, P. Intermedia*	Periodontal (HuGu cell)	LED blue light 435, 1000–1400 mW/cm^2, 1 menit	PS+/L-: 3.4 GQD: 3.8 PS-/L+: 5.2	76	%reduction in cell viability	(Pourhajibagher et al., 2019)
Curcumin 100 mg/L	Artificial biofilm: *A. actinomycetemcomitans* , *C. rectus, E. corrodens, F. nucleatum, P. gingivalis,* *P. intermedia, P. micra, T. denticola, T. forsythis*	Periodontal pocket model	LED laser 445 nm, 0,6 W 25% duty cycle 100 Hz, 10 s	curcumin + DMSO: 97.35 DMSO: 95.69 PS-/L+: 95.03	97.15	%reduction in cell viability	(Böcher et al., 2019)
Curcumin	*S. aureus*	Infected wounds in mice	LED blue light 450-470 nm, 120 J/cm^2, 40 min	control negative 11.84; 9.35; 0.8-	55.17; 26.85; 0- 0.2	%collagen; %fibroblasts;	(Tusi et al., 2015)

				1.1 PS-L+ 6.94; 25.29; 0.4-0.8 PS+L- 13.07; 24.49; 0.4-0.8		wound length in 6 days (cm)	
Curcumin 12.5 µg/ml (planktonic phase), 100 µg/ml (biofilm)	metronidazole resistance bacteria from subgingival plaque of periodontitis	Dental and mouth	LED blue light 450 nm, planktonic phase: 30 J/cm^2 biofilm: 120 J/cm^2	PS+L-: 0 (planktonic) 10^1 (biofilm)	100 (planktonic) 1.88 (biofilm)	%bacterial death log CFU/mL	(Zago et al., 2020)
Curcumin 100 µmol L^{-1}	*P. expansum*	Apple	LED 420 nm, 50watt, 15 min	PS+L-: 88.8 (in vitro); 100 (in vivo)	3.6 40.2	%spore survival rate % reduction in lesion	(Song et al., 2020)
Curcumin 0.5 µM	*E. coli* and coliform	Fresh fruit	LED 470 nm, 7.2 J /cm^2	100	10-20	%viability	(Zhang et al., 2020)
Curcumin 0.5-50 µM	generic *E. coli*	Fresh-cut apple	LED 420 nm, 298 mW/cm^2, 150-510 s	~6.6-7.2	~5.9-7.0	log CFU/g	(Tao et al., 2019)
Curcumin 1400 µM	resident fungi	Date	420 nm, 180-270 J /cm^2, 10 min	7 days (30°C); 28 days (4°C)	14 days (30°C) 98 days (4°C)	Survive fungal infection (day)	(Al-Asmari et al., 2018)
Curcumin 10 mg/L; aerosolization	*E. coli* O157:H7	Tomato, spinach, lettuce	UV-A 329-400 nm, 24 kJ/m^2, 5 min	6	~3	log CFU/cm^2	(Oliveira et al., 2018)
	L. innocua			5.7	2.4, ~3.5, 4.0	log CFU/cm^2	
Curcumin derivative SACUR-3 10-100 µM	generic *E. coli*	Tomato, cucumber, lettuce, fenugreek seeds, mung beans	LED 435 nm, 33.8 J/cm^2	8.4, 7.9, 7.7, 5.9, 6.1	2-5, 3.5-5, 1-5, 0.9-2.9, 2.5-4.1	log CFU/sample	(Glueck et al., 2017)
Curcumin 10 and 20 µM	Murine norovirus 1	Oysters	LED 470 nm, 3.6 J/cm^2	~4	2.9-3.2	log PFU/mL	(Wu et al., 2015)
Curcumin 10 µM	*V. parahaemolyticus*	Oysters	LED 470 nm, 3.6 J/cm^2,	5.0	0	log CFU/g	(Wu et al., 2016)

			1 min				
Curcumin 5-20 µM	generic *E. coli*	Oysters	LED 470 nm, 3.6 J/cm^2, 1 min	5	2.5-4.5	log CFU/g	(Y. Gao et al., 2019)
Curcumin 10 µM	total aerobic bacteria	Oysters	LED 470 nm, 5.4 J/cm^2, 1.5 min	~5	~5	log CFU/g	(Liu et al., 2016)
Curcumin 30 µM	total aerobic count	Sturgeon	LED 470 nm, 15 W, 1.5 min	4.64	1.19	log CFU/g	(Gong et al., 2020)
Curcumin 50 µM	total aerobic bacteria	Ready-to-eat salted jellyfish	LED 425 nm, 16 mW/cm^2, 15 min	Dark control 25 days	35 days	time to reach 3x10^4 CFU/g (threshold)	(Hu et al., 2019)
Curcumin 0.75 mg/mL water soluble salt	*S. aureus*	Coalho cheese	LED 450 nm, 16-100 J/cm^2, 5-30 min	~5.5	~1.0	log CFU/g	(Santos et al., 2019)
		Unpasteurized milk		~5.5	~5.1-5.2		
novaSol®-curcumin 100 µM	*S. aureus*	Chicken leg	LED 435 nm, 33.8 J/cm^2	7.2	5.5	log CFU/g	(Tortik et al., 2014)
Curcumin 300 ppm	*L. monocytogenes*	Chicken skin	LED 430 nm, 32.1 kJ/m^2, 2.5 min	5.3	2.4	log CFU/cm^2	(Gao & Matthews, 2020)
	Salmonella			~5.0	~3.5		
Curcumin containing cassava-gelatin hydrogel	*L. innocua*	Cooked sausage	UV-A 320-400 nm, 32 W/m^2, 5-30 min, 4°C	4-6	1	log CFU/mL	(Tosati et al., 2018)
Curcumin 50 µM	*S. aureus* (biofilm)	Food contact surfaces	LED 460-465 nm, 10 min	5.6	0	log CFU/mL	(Li et al., 2020)
Curcumin 0.015%	*P. acnes*	Acne vulgaris	LED blue light 423 nm, 2270 lux, 30 min	100	20.5	% inhibition	(Djalil et al., 2023)
Hypericin							
Hypericin 15 µM	*B. cereus*	Apricot, plum, cauliflower	LED 585 nm, 6.8 J/cm^2, 30 min	5.7, 6, 6.3	4.6, 5.2, 5.2	log CFU/g	(Aponiene et al., 2015)
	mesophilic microorganisms			~6.0, ~6.2, ~6.7	5.3, 5.5, ~6.1		
Hypericin 0.25 µM	MSSA	Chronic infections	LED 602 nm, 8 J/cm^2, 10 min	6	0	log CFU/mL	(García et al., 2015)
Hypericin 1 µM	MRSA			6	0		
Hypericin 1 µM	MSSA biofilms		LED 602 nm, 25 J/cm^2,	7-8	5-6		

	MRSA biofilms		30 min	7	~4		
PVP-hypericin 100 nM	*S. aureus*		Waldmann PDT 1200 red light, 75 mW/cm^2, 30 min	8-9	3-4	log CFU	(Engelhardt et al., 2010)
Hypericin 8 µM	MSSA, MRSA, *E. Coli*		600-800 nm, 30 J/cm^2, 30 min	0	>6, >6, <0.2	log unit reduction	(Yow et al., 2012)
Riboflavin							
Riboflavin-tryptophan gel	*P. acne*	Acne vulgaris	LED blue light 415 nm, 48 J/cm^2, 20 min	0%	25.7% (7 weeks)	%patients achieving GAAS (7 weeks)	(Wangsuwan & Meephansan, 2019)
				21.67	14.39	acne lesion counts	
Riboflavin 50 µM	intracellular HIV	Platelet concentrates	UV light Mirasol PRT, lamp phosphor 265 to 370 nm, 6.2 J per mL, 8-10 min	-	4.46 ± 0.39	log reduction factors	(Goodrich et al., 2004)
	cells associated HIV				5.93 ± 0.20		
	west nile virus				5.19 ± 0.50		
	nonenveloped porcine parvovirus				>5.0		
Riboflavin 100 µM	colistin-resistant *P. aeruginosa:* PA1, PA2 isolate	Infection in humans	LED blue light 420-480 nm, 1200 mW/cm^2, 120 s	0	PA1: 0.43 PA2: 0.34	MIC (µg/mL)	(Najari et al., 2024)
Riboflavin 0.01%	MRSA	Infection in humans	LED blue light 450 nm, 46.6 mW/cm^2, 30 min	PS-L+ = 70	99.5	%elimination	(Makdoumi et al., 2019)
Riboflavin-5-phosphate 0,1%	*P. aeruginosa, S. aureus, S. epidermidis*	Infectious keratitis	UVA 365 nm, 3 mW/cm^2, 1h	5.27, 11.3, 8.44	7.62, 29.45, 32.37	growth inhibition zone (GIZ, mm^2)	(Martins et al., 2008)
	Resistant bacteria: MRSA, PRPA ORSE, PRSP			9.41, 0.36, 5.59, 12.89	25.51, 3.26, 21.84, 21.46		
	C. albicans			-	0		
Riboflavin 0.1%	*S. aureus,* MRSA, *P. aeruginosa*	Infectious corneal ulcers	UV light 365 nm	PS-L+; PS+L- no bacterial	bacterial death	bacterial death	(Schrier et al., 2009)

				death			
Riboflavi -5-phosphate 0.1 %	*C. albicans, F. solani*	Infectious keratitis	UV A (365 nm), 3 mW/cm^2, 30 min	Blank = 7.06, 7.04 PS-L+ = 6.74, 7.06 PS+L- = 7.05, 6.72	6.79, 6.80	cell diameter (µm)	(Kashiwabuchi et al., 2013)
Riboflavin 500 mM, 35 mL	*P. falciparum* (in vitro)	Plasma and platelet conc	UV Mirasol PRT 6.24 J/ml, 5-10 min	-	>3.2	log reduction	(Keil et al., 2013)
Riboflavin 500 mM, 320 µL	*P. yoelii* (in vivo)				>4.4		
Riboflavin 500 mM, 35 mL	*B. microti*	Whole blood	UV 80 J/ml$_{RBC}$, 40 min	-	>5	log reduction	(Tonnetti et al., 2013)
Riboflavin 50 µM	*E. coli*	Nosocomial infections	white light, 38.6 W/m², 2h	PS+L-: no change in absorption maxima	get loss of its absorption maxima	absorption spectra	(Khan et al., 2019)
				PS+L-/PS-L+: no significant ROS generation	significant ROS generation	ROS formation, lipid	
				PS+L-/PS-L+: ±5	±65	peroxidation MDA level (mmol/ml)	
				PS+L-/PS-L+: ±80, ±100, ±0.24, ±95	SOD ±30 catalase ±20 GSH activity ±0.6 GSH level ±23	U/mg U/mg µmol/min/mg protein %	
				PS+L-/PS-L+: ±145-150	LDH activity ±100	µU/ml	

				PS-L+: ±6.9 PS+L-: ±7	bacterial death ±2.6	log CFU/ml	
Riboflavin + UVA +: voriconazole 10 mg/mL/ amphotericin B 1.5 mg/mL/ chlorhexidine 0.02%	*A. terreus, A. fumigatus, A. flavus, F. Solani, F. falciforme, F. Proliferatum*	Mycotic keratitis	UVA 365 nm, 9 mW/cm^2, 10 min	Pretreatment=5	no fungal growth	CFU/mL	(Kunt et al., 2020)
Riboflavin 50 µM	vesicular stomatitis, herpes simplex, and polio virus	Blood platelet	UV 200-365 nm,0.00203 W/cm^2, 10 min	UV alone 2.77 log 10	4.06, 4.27, 2.6	log titer reduction	(Mirshafiee et al., 2015)
Riboflavin 50 µM	MRSA, MDR *E. coli*, MRSA in mix culture, MDR *E. coli* in mix culture	Persistent infections	Blue LED light 450 nm	MRSA, MDRE PS+L-: no effect PS-L+: little reduction of cells	4, 5, 5, 7	log reduction	(Banerjee et al., 2020)
					increased ~14.8, ~16.8, ~16.3,~16.3	fluorescence intensity of DCF	
					increased ~3.8, 4.33, ~3.92, ~3.92	lipid peroxidation	
					34, 34, 50, 50%	inhibition of biofilm	
Riboflavin 50 µM	*L. donovani infantum*	Plasma and platelet conc.	UV 265-370 nm, 5-9 J/cm^2, 10 min (6-24 J/ml)	-	5 of 6 plasma unit 5 of 6 platelets	log reduction	(Cardo et al., 2006)
Riboflavin 50 µM	dengue viruses (DENV 1-4)	Blood transfusion	UV 9.1 J/ml, Mirasol PRT system		1.28, 1.45, 1.71, 1.81	log reduction	(Faddy et al., 2016)
Riboflavin 0.015%	*P. acnes*	Acne vulgaris	LED blue light 423 nm, 2270 lux, 30 min		33.8	%inhibition	(Djalil et al., 2023)
Riboflavin 266 µmol L^{-1}	*A. actinomycetemcomitans, C. albicans, E. faecalis, E. coli, L. paracasei, P. gingivalis,*	Periodontal	LED blue light 460 nm, power: 0.4 W; fluence: 37.7 J/cm^2; fluence rate: 0.63 W/cm^2), 1 min	PS-L+: *P. gingivalis, P. intermedia* = full kills	1.11, ~0, 0.37, ~0, 1.36, full kills, full kills, 0.37	log reduction	(Nielsen et al., 2015b)

	P. intermedia, P. acnes						
Riboflavin 0.1%	*Tulane virus*	Blueberrie	405-nm light, 4.2 mW/cm^2, 30 min	PS-L- = +0.06 PS+L- = -0.13	-0.51	log reduction	(Kingsley et al., 2018)
β-carotene 0.015%	*P. acnes*	Acne vulgaris	LED blue light 423 nm, 2270 lux, 30 min		41.9	%inhibition	(Djalil et al., 2023)
Chlorophyll Derivatives							
Not coperized chlorophyll sodium salt 1.5x10^{-4} M	*total aerobic mesophilic bacteria* *L. monocytogenes*	Cherry tomatoes	LED 405 nm, 10 mW/cm^2, 5 min	water: 0.8, 0.6 PS+L-: 0 PS-L+: 0	2.4 (99.5%) 1.6 (95%)	log reduction (%inhibition)	(Paskeviciute et al., 2018)
Na-Chl 1 mM	*L. monocytogenes,* naturally occurring yeasts, mesophiles	Strawberry	visible light 400 nm, 12 mW/cm^2, 20 min	PS+L-/PS-L+: not affect	98, 86, 97 extended 2 days, increased by 19% no impact	%inhibition shelf life total antioxidant, phenol, anthocyanins, surface colour	(Luksiene & Paskeviciute, 2011)
Chl 1.5 ×10^{-5} M, CHS 0.1%, Chl-CHS complex	*Salmonella enterica* yeasts/molds	Strawberry	visible light 405 nm, 38 J/cm^2		1.8, 2.15, 7 0.9, 0.4, 1.4	log reduction	(Buchovec et al., 2016)
Chl 1.5×10^{-5} M	*E. coli*	Wheat seeds	LED 405 nm, 30 J/cm^2, 50 min	PS-L+/PS+L-: no impact	~95	% reduction	(Žudytė & Lukšienė, 2019)
Chl 1.5×10^{-3} M	*F. oxysporum*		LED 405 nm, 18 J/cm^2		74%	growth delay	
Na-Chl 7.5x10^{-7} M	*B. cereus, L. monocytogenes,* thermoresistant strains *B. cereus,* thermoresistant *L. monocytogenes*	Surface sanitation (polyolefine)	LED 405 nm, 12 mW/cm^2	7, 7, 7, 7	0 (5 min), 0 (±5-10 min), 0 (> 30 min), 0 (>>30 min)	log CFU/ml	(Luksiene & Paskeviciute, 2011)
Na-Chl 1.5 x10^{-4} M	*L. monocytogenes*		LED 405 nm, 12	4.5	0	log CFU/cm^2	

	biofilms		mW/cm^2, 5 min				
Na-Chl 7.5x10^{-5} M	*Bacillus* spores attached to the surface of polyolefine			6	1	log CFU/cm^2	
Chlorin-e6 200 mM	Biofilm: *S. oralis*, *P. gingivalis*, *A. actinomycetemcomitans*	Periodontitis	blue light 450 nm, 30 J/cm^2, 22 min		8.46 log10, 8.24 log10, 4.01 log10	bacterial elimination	(Carvalho et al., 2020)
	F. nucleatum		red light 660 nm, 30 J/cm^2, 26 min		3.46 log 10		
Chlorin e6 trisodium salt 1 M (planktonic assay), 10 M (biofilm assay)	*M. catarrhalis*, *S. pneumoniae*, nontypeable *Haemophilus influenzae*	Otitis media	LED 405 ±10-nm, 100 mW/cm^2, 2 min (planktonic), 15 min (biofilm)	planktonic cultures ±10^7, ±10^7, ±10^8 biofilms ±10^6, ±10$^{5.5}$, ±10^7	planktonic cultures 0, <10$^{0.5}$, ±10^3 biofilms ±10$^{2.5}$, ±10$^{0.5}$, 0	CFU/ml	(Luke-Marshall et al., 2020)
Chlorin e6 200 µM	*S. mutans* biofilms	Dental	LED red light 660 nm, 19 mW/cm^2, 13.25 min	±8 ±2 mM	±3 ±0.1 mM	Log CFU biofilm lactic acid	(Nie et al., 2020)
Chlorin e6 100 µg/ml	*P. acnes*	Skin disease	halogen 30,000 lx, 30 min	>31.25 µg/ml	>0.49 µg/ml	MIC$_{99}$ value	(Jeon et al., 2015)

UV-A: ultraviolet A; LED: light-emitting diode; ROS: reactive oxygen species; PS: photosensitizer; L: light; MSSA: methicillin-susceptible *S. aureus*; MRSA: methicillin-resistant *S. Aureus*; Chl: chlorophyllin, CHS: chitosan

In contrast to natural chlorophyll, chlorophyllin (**Figure 3**) is a water-soluble semi-synthetic porphyrin that is used as a food colorant and additive (E141ii). It is widely used in cosmetics and nutritional supplements (López-Carballo et al. 2008). A previous study has confirmed that copper-free chlorophyllin exhibits photosensitizing properties. It can inhibit the growth of major food pathogens, such as *Bacillus cereus*, *Salmonella enterica*, *Listeria monocytogenes*, *Escherichia coli*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*, when exposed to blue light (405 nm) (Luksiene and Paskeviciute, 2011a; Luksiene and Paskeviciute, 2011b), as well as numerous harmful microfungi (Luksiene and Paskeviciute, 2011b).

Antimicrobial Mechanisms of PDI

PDI has been shown to inhibit harmful microorganisms, bacteria, viruses, fungi, plankton cells, biofilms, vegetative cells, and endospores. The process of photosensitizer uptake is determined by the cell wall structure of the microorganisms (**Figure 6**). In addition, the characteristics of photosensitizers determine the amount of uptake by microorganisms.

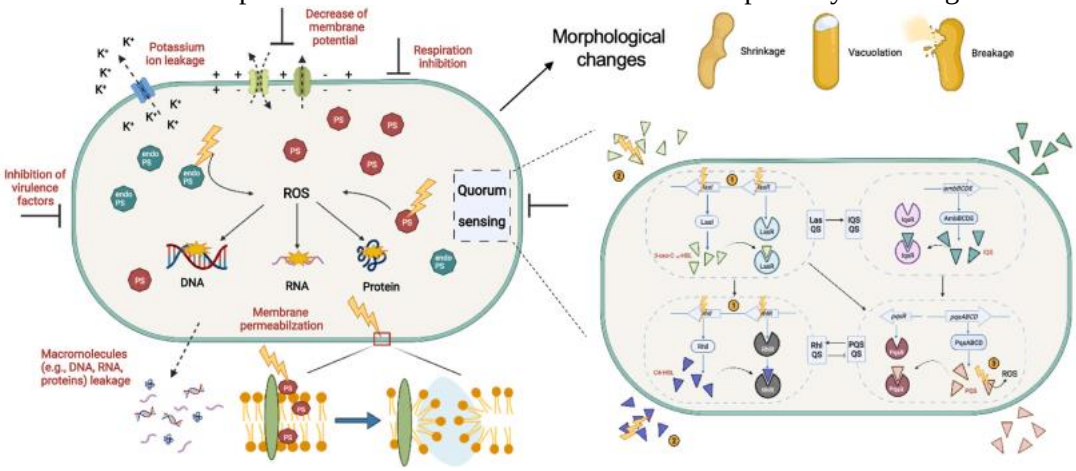

Figure 6. PDI mechanisms for microbial destruction

The cell wall of gram-positive bacteria is composed of negatively charged teichoic and lipoteichoic acids as well as a thick yet porous layer of peptidoglycan. However, gram-negative bacteria have an outer membrane that is well organized and includes lipopolysaccharides that are negatively charged and maintained by cationic ions such as Mg^{2+} or Ca^{2+} (George et al., 2009). Generally, gram-positive bacteria are more susceptible to PDI than gram-negative bacteria because of variations in the cell wall structure. Biofilm cells are more resistant to PDI than plankton cells because of extracellular polymer protection. In viruses, the phospholipid layer and the viral protein on the locked biofilm cells make them more susceptible to PDI than the unlocked virus (Willis et al., 2021). In fungi, a porous layer of chitin, β-glucan, and mannan is present in the fungal cell wall. Compared to Gram-positive and Gram-negative bacteria, the fungus's cell wall possesses an intermediate permeability and a negative/neutral charge (Luksiene, 2021). Intracellular accumulation is driven by self-promoted uptake pathways and electrostatic interactions (George et al. 2009). Similarly, cationic photosensitizers and negatively charged fungal cell walls interact via electrostatic interactions (Luksiene, 2021). However, fungi are generally less susceptible to PDI than bacteria because of their larger size and lower risk of DNA damage in the presence of nuclear membranes (Luksiene, 2021).

For PS to function as an efficient antibacterial agent, it must pass through the bacterial cell walls and enter the cytoplasm or plasma membrane. However, the easy diffusion of PS into the bacterial cytoplasm is hampered by the obstacles found in bacterial cell membranes. Because of their membrane barrier, which prevents anionic and neutral PSs from being absorbed, it is more challenging to design highly effective PS for mediating PDI (Pérez-

Laguna et al., 2018). In an effort to enhance the chemical structure of PS, cationic (positively charged) PS are created, or they are coupled or combined with positively charged substances, such as poly-L-lysine, polyethyleneimine, and polymyxin B (Sperandio et al., 2013; Valle et al., 2020).

CONCLUSION

Natural photosensitizers, such as curcumin, hypericin, riboflavin, and chlorophyll derivatives, have been extensively researched, particularly in their application in the food sector and antimicrobial pharmaceutics through the PDI technique. Their application in the treatment of diseases can be enhanced by formulating various dosage forms and combinations of antimicrobial agents.

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REFERENCES

Abrahamse, H., & Hamblin, M. R. (2016). New photosensitizers for photodynamic therapy. *The Biochemical Journal*, *473*(4), 347–364. https://doi.org/10.1042/BJ20150942

Aghajanzadeh, S., Ziaiifar, A. M., & Verkerk, R. (2023). Effect of thermal and non-thermal treatments on the color of citrus juice: A review. *Food Reviews International*, *39*(6), 3555–3577. https://doi.org/10.1080/87559129.2021.2012799

Agostinis, P., Berg, K., Cengel, K. A., Foster, T. H., Girotti, A. W., Gollnick, S. O., Hahn, S. M., Hamblin, M. R., Juzeniene, A., Kessel, D., Korbelik, M., Moan, J., Mroz, P., Nowis, D., Piette, J., Wilson, B. C., & Golab, J. (2011). Photodynamic therapy of cancer: an update. *CA: A Cancer Journal for Clinicians*, *61*(4), 250–281. https://doi.org/10.3322/caac.20114

Al-Asmari, F., Mereddy, R., & Sultanbawa, Y. (2017). A novel photosensitization treatment for the inactivation of fungal spores and cells mediated by curcumin. *Journal of Photochemistry and Photobiology B: Biology*, *173*, 301–306. https://doi.org/10.1016/j.jphotobiol.2017.06.009

Al-Asmari, F., Mereddy, R., & Sultanbawa, Y. (2018). The effect of photosensitization mediated by curcumin on storage life of fresh date (Phoenix dactylifera L.) fruit. *Food Control*, *93*, 305–309. https://doi.org/10.1016/j.foodcont.2018.06.005

Allison, R., Moghissi, K., Downie, G., & Dixon, K. (2011). Photodynamic therapy (PDT) for lung cancer. *Photodiagnosis and Photodynamic Therapy*, *8*(3), 231–239. https://doi.org/10.1016/j.pdpdt.2011.03.342

Allison, R. R., & Bansal, S. (2022). Photodynamic therapy for peripheral lung cancer. *Photodiagnosis and Photodynamic Therapy*, *38*, 102825. https://doi.org/10.1016/j.pdpdt.2022.102825

Allison, R. R., & Moghissi, K. (2013). Photodynamic Therapy (PDT): PDT Mechanisms. In *Clinical endoscopy* (Vol. 46, Issue 1). https://doi.org/10.5946/ce.2013.46.1.24

Alwaeli, H. A., Al-Khateeb, S. N., & Al-Sadi, A. (2015). Long-term clinical effect of adjunctive antimicrobial photodynamic therapy in periodontal treatment: a randomized clinical trial. *Lasers in Medical Science*, *30*(2), 801–807. https://doi.org/10.1007/s10103-013-1426-y

Aponiene, K., Paskeviciute, E., Reklaitis, I., & Luksiene, Z. (2015). Reduction of microbial contamination of fruits and vegetables by hypericin-based photosensitization: Comparison with other emerging antimicrobial treatments. *Journal of Food Engineering*, *144*, 29–35. https://doi.org/10.1016/j.jfoodeng.2014.07.012

Araújo, N. C., De Menezes, R. F., Carneiro, V. S. M., Dos Santos-Neto, A. P., Fontana, C. R., Bagnato, V. S., Harvey, C. M., & Gerbi, M. E. M. (2017). Photodynamic Inactivation of Cariogenic Pathogens Using Curcumin as Photosensitizer.

Photomedicine and Laser Surgery, *35*(5), 259–263. https://doi.org/10.1089/pho.2016.4156

Banerjee, S., Ghosh, D., Vishakha, K., Das, S., Mondal, S., & Ganguli, A. (2020). Photodynamic antimicrobial chemotherapy (PACT) using riboflavin inhibits the mono and dual species biofilm produced by antibiotic resistant Staphylococcus aureus and Escherichia coli. *Photodiagnosis and Photodynamic Therapy*, *32*, 102002. https://doi.org/10.1016/j.pdpdt.2020.102002

Barra, F., Roscetto, E., Soriano, A. A., Vollaro, A., Postiglione, I., Pierantoni, M. G., Palumbo, G., & Catania, M. R. (2015). Photodynamic and antibiotic therapy in combination to fight biofilms and resistant surface bacterial infections. *International Journal of Molecular Sciences*, *16*(9), 20417–20430. https://doi.org/10.3390/ijms160920417

Bhavya, M. L., & Hebbar, H. U. (2019). Sono-photodynamic inactivation of Escherichia coli and Staphylococcus aureus in orange juice. *Ultrasonics Sonochemistry*, *57*, 108–115. https://doi.org/10.1016/j.ultsonch.2019.05.002

Böcher, S., Wenzler, J.-S., Falk, W., & Braun, A. (2019). Comparison of different laser-based photochemical systems for periodontal treatment. *Photodiagnosis and Photodynamic Therapy*, *27*, 433–439. https://doi.org/10.1016/j.pdpdt.2019.06.009

Boen, M., Brownell, J., Patel, P., & Tsoukas, M. M. (2017). The Role of Photodynamic Therapy in Acne: An Evidence-Based Review. *American Journal of Clinical Dermatology*, *18*(3), 311–321. https://doi.org/10.1007/s40257-017-0255-3

Bogdan, C. (2020). Macrophages as host, effector and immunoregulatory cells in leishmaniasis: Impact of tissue micro-environment and metabolism. *Cytokine: X*, *2*(4), 100041. https://doi.org/10.1016/j.cytox.2020.100041

Buchovec, I., Lukseviciute, V., Marsalka, A., Reklaitis, I., & Luksiene, Z. (2016). Effective photosensitization-based inactivation of Gram (−) food pathogens and molds using the chlorophyllin—chitosan complex: towards photoactive edible coatings to preserve strawberries. *Photochemical & Photobiological Sciences*, *15*(4), 506–516. https://doi.org/10.1039/c5pp00376h

Bustamante, V., & Palavecino, C. E. (2023). Effect of photodynamic therapy on multidrug-resistant Acinetobacter baumannii: A scoping review. *Photodiagnosis and Photodynamic Therapy*, *43*, 103709. https://doi.org/10.1016/j.pdpdt.2023.103709

Cardo, L. J., Rentas, F. J., Ketchum, L., Salata, J., Harman, R., Melvin, W., Weina, P. J., Mendez, J., Reddy, H., & Goodrich, R. (2006). Pathogen inactivation of Leishmania donovani infantum in plasma and platelet concentrates using riboflavin and ultraviolet light. *Vox Sanguinis*, *90*(2), 85–91. https://doi.org/10.1111/j.1423-0410.2005.00736.x

Carvalho, V. F., Andrade, P. V. C., Rodrigues, M. F., Hirata, M. H., Hirata, R. D. C., Pannuti, C. M., De Micheli, G., & Conde, M. C. (2015). Antimicrobial photodynamic effect to treat residual pockets in periodontal patients: a randomized controlled clinical trial. *Journal of Clinical Periodontology*, *42*(5), 440–447. https://doi.org/10.1111/jcpe.12393

Chi, Y. F., Qin, J. J., Li, Z., Ge, Q., & Zeng, W. H. (2020). Enhanced anti-tumor efficacy of 5-aminolevulinic acid-gold nanoparticles-mediated photodynamic therapy in cutaneous squamous cell carcinoma cells. *Brazilian Journal of Medical and Biological Research = Revista Brasileira de Pesquisas Medicas e Biologicas*, *53*(5), e8457. https://doi.org/10.1590/1414-431x20208457

Cieplik, F., Deng, D., Crielaard, W., Buchalla, W., Hellwig, E., Al-Ahmad, A., & Maisch, T. (2018). Antimicrobial photodynamic therapy–what we know and what we don't. *Critical Reviews in Microbiology*, *44*(5), 571–589. https://doi.org/10.1080/1040841X.2018.1467876

Comacchi, C., Bencini, P. L., Galimberti, M. G., Cappugi, P., & Torchia, D. (2012). Topical photodynamic therapy for idiopathic hirsutism and hypertrichosis. *Plastic and Reconstructive Surgery*, *129*(6), 1012e-1014e. https://doi.org/10.1097/PRS.0b013e31824f00cc

Correia, J. H., Rodrigues, J. A., Pimenta, S., Dong, T., & Yang, Z. (2021). Photodynamic therapy review: Principles, photosensitizers, applications, and future directions. *Pharmaceutics*, *13*(9), 1–16. https://doi.org/10.3390/pharmaceutics13091332

Cosgarea, R., Pollmann, R., Sharif, J., Schmidt, T., Stein, R., Bodea, A., Auschill, T., Sculean, A., Eming, R., Greene, B., Hertl, M., & Arweiler, N. (2020). Photodynamic therapy in oral lichen planus: A prospective case-controlled pilot study. *Scientific Reports*, *10*(1), 1667. https://doi.org/10.1038/s41598-020-58548-9

Cossu, M., Ledda, L., & Cossu, A. (2021). Emerging trends in the photodynamic inactivation (PDI) applied to the food decontamination. *Food Research International*, *144*, 110358. https://doi.org/10.1016/j.foodres.2021.110358

Dąbrowski, J. M., Pucelik, B., Regiel-Futyra, A., Brindell, M., Mazuryk, O., Kyzioł, A., Stochel, G., Macyk, W., & Arnaut, L. G. (2016). Engineering of relevant photodynamic processes through structural modifications of metallotetrapyrrolic photosensitizers. *Coordination Chemistry Reviews*, *325*, 67–101. https://doi.org/10.1016/j.ccr.2016.06.007

Dai, T., Huang, Y.-Y., & Hamblin, M. R. (2009). Photodynamic therapy for localized infections—State of the art. *Photodiagnosis and Photodynamic Therapy*, *6*(3), 170–188. https://doi.org/10.1016/j.pdpdt.2009.10.008

Danial Mohabati Elon HC van Dijk, T. J. van R. E. K. de J. M. B. B. J. P. M.-C. G. D. C. B. H. S. F. S. Y., & Boon, C. J. F. (2018). Clinical spectrum of severe chronic central serous chorioretinopathy and outcome of photodynamic therapy. *Clinical Ophthalmology*, *12*, 2167–2176. https://doi.org/10.2147/OPTH.S174573

Djalil, A. D., Susanto, A. P., Arisugita, R. N., Dhiani, B. A., Maulidan, M. F., & Zamzani, I. (2023). *Natural Dyes as Photosensitizers of Propionibacterium acnes* (Vol. 2022). Atlantis Press International BV. https://doi.org/10.2991/978-94-6463-322-1_20

Doeveren, T. E. M., Karakullukçu, M. B., van Veen, R. L. P., Lopez-Yurda, M., Schreuder, W. H., & Tan, I. B. (2018). Adjuvant photodynamic therapy in head and neck cancer after tumor-positive resection margins. The Laryngoscope, 128(3), 657–663. https://doi.org/10.1002/lary.26792

Dolmans, D. E. J. G. J., Fukumura, D., & Jain, R. K. (2003). Photodynamic therapy for cancer. *Nature Reviews. Cancer*, *3*(5), 380–387. https://doi.org/10.1038/nrc1071

Dong, Y., Cao, W., & Cao, J. (2021). Treatment of rheumatoid arthritis by phototherapy: advances and perspectives. *Nanoscale*, *13*(35), 14591–14608. https://doi.org/10.1039/D1NR03623H

Dougherty, T. J., Gomer, C. J., Henderson, B. W., Jori, G., Kessel, D., Korbelik, M., Moan, J., & Peng, Q. (1998). Photodynamic therapy. *Journal of the National Cancer Institute*, *90*(12), 889–905. https://doi.org/10.1093/jnci/90.12.889

Engelhardt, V., Krammer, B., & Plaetzer, K. (2010). Antibacterial photodynamic therapy using water-soluble formulations of hypericin or mTHPC is effective in inactivation of Staphylococcus aureus. *Photochemical and Photobiological Sciences*, *9*(3), 365–369. https://doi.org/10.1039/b9pp00144a

Espeland, K., Kleinauskas, A., Juzenas, P., Darvekar, S., Vasovic, V., Warloe, T., Christensen, E., Jahnsen, J., & Peng, Q. (2023). Photodynamic Effects with 5-Aminolevulinic Acid on Cytokines and Exosomes in Human Peripheral Blood Mononuclear Cells from Patients with Crohn's Disease. *International Journal of Molecular Sciences*, *24*(5). https://doi.org/10.3390/ijms24054554

Faddy, H. M., Fryk, J. J., Watterson, D., Young, P. R., Modhiran, N., Muller, D. A., Keil, S. D., Goodrich, R. P., & Marks, D. C. (2016). Riboflavin and ultraviolet light: impact on dengue virus infectivity. *Vox Sanguinis*, *111*(3), 235–241. https://doi.org/10.1111/vox.12414

Fast, L. D., DiLeone, G., Cardarelli, G., Li, J., & Goodrich, R. (2006). Mirasol PRT treatment of donor white blood cells prevents the development of xenogeneic graft-versus-host disease in Rag2-/-gamma c-/- double knockout mice. *Transfusion*, *46*(9), 1553–1560. https://doi.org/10.1111/j.1537-2995.2006.00939.x

Fehr, M. K., Hornung, R., Degen, A., Schwarz, V. A., Fink, D., Haller, U., & Wyss, P. (2002). Photodynamic therapy of vulvar and vaginal condyloma and intraepithelial neoplasia using topically applied 5-aminolevulinic acid*. *Lasers in Surgery and Medicine*, *30*(4), 273–279. https://doi.org/https://doi.org/10.1002/lsm.10048

Gao, J., & Matthews, K. R. (2020). Effects of the photosensitizer curcumin in inactivating foodborne pathogens on chicken skin. *Food Control*, *109*, 106959. https://doi.org/10.1016/j.foodcont.2019.106959

Gao, Y., Wu, J., Li, Z., Zhang, X., Lu, N., Xue, C., Leung, A. W., Xu, C., & Tang, Q. (2019). Curcumin-mediated photodynamic inactivation (PDI) against DH5α contaminated in oysters and cellular toxicological evaluation of PDI-treated oysters. *Photodiagnosis and Photodynamic Therapy*, *26*, 244–251. https://doi.org/10.1016/j.pdpdt.2019.04.002

Garcia-Lara, G., Linares-González, L., Ródenas-Herranz, T., & Ruiz-Villaverde, R. (2020). Chilblain-like lesions in pediatrics dermatological outpatients during the COVID-19 outbreak. *Dermatologic Therapy*, *33*(5), e13516. https://doi.org/10.1111/dth.13516

Garcia de Carvalho, G., Sanchez-Puetate, J. C., Donatoni, M. C., Maquera Huacho, P. M., de Souza Rastelli, A. N., de Oliveira, K. T., Palomari Spolidorio, D. M., & Leal Zandim-Barcelos, D. (2020). Photodynamic inactivation using a chlorin-based photosensitizer with blue or red-light irradiation against single-species biofilms related to periodontitis. *Photodiagnosis and Photodynamic Therapy*, *31*, 101916. https://doi.org/10.1016/j.pdpdt.2020.101916

García, I., Ballesta, S., Gilaberte, Y., Rezusta, A., & Pascual, Á. (2015). Antimicrobial photodynamic activity of hypericin against methicillin-susceptible and resistant Staphylococcus aureus biofilms. *Future Microbiology*, *10*(3), 347–356. https://doi.org/10.2217/FMB.14.114

George, S., Hamblin, M. R., & Kishen, A. (2009). Uptake pathways of anionic and cationic photosensitizers into bacteria. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *8*(6), 788–795. https://doi.org/10.1039/b809624d

Ghate, V. S., Zhou, W., & Yuk, H.-G. (2019). Perspectives and Trends in the Application of Photodynamic Inactivation for Microbiological Food Safety. *Comprehensive Reviews in Food Science and Food Safety*, *18*(2), 402–424. https://doi.org/10.1111/1541-4337.12418

Gil-Pallares, P., Gracia-Cazaña, T., Álvarez-Salafranca, M., Gorgojo, M. A., García-García, M., Beltrán-Rosel, A., Almenara-Blasco, M., Navarro-Bielsa, A., & Gilaberte, Y. (2024). Cutaneous Alternariosis in Immunosuppressed Patients Treated with Photodynamic Therapy and Oral Antifungals, a Synergistic Strategy. *Pharmaceuticals*, *17*(2). https://doi.org/10.3390/ph17020245

Glueck, M., Schamberger, B., Eckl, P., & Plaetzer, K. (2017). New horizons in microbiological food safety: Photodynamic Decontamination based on a curcumin derivative. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *16*(12), 1784–1791. https://doi.org/10.1039/c7pp00165g

Gong, C., Li, Y., Gao, R., Xiao, F., Zhou, X., Wang, H., Xu, H., Wang, R., Huang, P., & Zhao, Y. (2020). Preservation of sturgeon using a photodynamic non-thermal disinfection technology mediated by curcumin. *Food Bioscience*, *36*, 100594. https://doi.org/10.1016/j.fbio.2020.100594

Goodrich, R. P., Ruane, P. H., Edrich, R., Gampp, D., Keil, S. D., & Lynne Leonard, R. (2004). Photochemical inactivation of selected viruses and bacteria in platelet concentrates using riboflavin and light. *Transfusion*, *44*(6), 877–885.

Hamblin, M. R. (2020). Photodynamic Therapy for Cancer: What's Past is Prologue. *Photochemistry and Photobiology*, *96*(3), 506–516. https://doi.org/10.1111/php.13190

Hamblin, M. R., & Huang, Y. (Eds.). (2017). *Imaging in Photodynamic Therapy* (1st ed.). Taylor & Francis. https://doi.org/10.1201/b21922

Henderson, B. W., & Dougherty, T. J. (1992). How Does Photodynamic Therapy Work? *Photochemistry and Photobiology*, *55*(1), 145–157. https://doi.org/10.1111/j.1751-1097.1992.tb04222.x

Hu, J., Zhou, F., Lin, Y., Zhou, A., Tan, B. K., Zeng, S., Hamzah, S. S., & Lin, S. (2019). The effects of photodynamically activated curcumin on the preservation of low alum treated ready-to-eat jellyfish. *Lwt*, *115*(June). https://doi.org/10.1016/j.lwt.2019.108443

Huang, H.-C., Rizvi, I., Liu, J., Anbil, S., Kalra, A., Lee, H., Baglo, Y., Paz, N., Hayden, D., Pereira, S., Pogue, B. W., Fitzgerald, J., & Hasan, T. (2018). Photodynamic Priming Mitigates Chemotherapeutic Selection Pressures and Improves Drug Delivery. *Cancer Research*, *78*(2), 558–571. https://doi.org/10.1158/0008-5472.CAN-17-1700

Jeon, Y. M., Lee, H. S., Jeong, D., Oh, H. K., Ra, K. H., & Lee, M. Y. (2015). Antimicrobial photodynamic therapy using chlorin e6 with halogen light for acne bacteria-induced inflammation. *Life Sciences*, *124*, 56–63. https://doi.org/10.1016/j.lfs.2014.12.029

Jerjes, W., Stevenson, H., Ramsay, D., Hamdoon, Z., & Hopper, C. (2022). Quality of life following photodynamic therapy for head and neck pathologies: An exploratory study. *Photodiagnosis and Photodynamic Therapy*, *38*, 102800. https://doi.org/10.1016/j.pdpdt.2022.102800

Jerjes, W., Upile, T., Hamdoon, Z., Mosse, C. A., Akram, S., & Hopper, C. (2011). Photodynamic therapy outcome for oral dysplasia. *Lasers in Surgery and Medicine*, *43*(3), 192–199. https://doi.org/10.1002/lsm.21036

Kairyte, K., Lapinskas, S., Gudelis, V., & Luksiene, Z. (2012). Effective inactivation of food pathogens Listeria monocytogenes and Salmonella enterica by combined treatment of hypericin-based photosensitization and high power pulsed light. *Journal of Applied Microbiology*, *112*(6), 1144–1151. https://doi.org/10.1111/j.1365-2672.2012.05296.x

Kashef, N., Huang, Y.-Y., & Hamblin, M. R. (2017). No Title. *Nanophotonics*, *6*(5), 853–879. https://doi.org/doi:10.1515/nanoph-2016-0189

Kashiwabuchi, R. T., Carvalho, F. R. S., Khan, Y. A., Hirai, F., Campos, M. S., & McDonnell, P. J. (2013). Assessment of fungal viability after long-wave ultraviolet light irradiation combined with riboflavin administration. *Graefe's Archive for Clinical and Experimental Ophthalmology*, *251*(2), 521–527. https://doi.org/10.1007/s00417-012-2209-z

Kawczyk-Krupka, A., Pucelik, B., Międzybrodzka, A., Sieroń, A. R., & Dąbrowski, J. M. (2018). Photodynamic therapy as an alternative to antibiotic therapy for the treatment of infected leg ulcers. *Photodiagnosis and Photodynamic Therapy*, *23*, 132–143. https://doi.org/10.1016/j.pdpdt.2018.05.001

Keil, S. D., Kiser, P., Sullivan, J. J., Kong, A. S., Reddy, H. L., Avery, A., & Goodrich, R. P. (2013). Inactivation of Plasmodium spp. in plasma and platelet concentrates using riboflavin and ultraviolet light. *Transfusion*, *53*(10), 2278–2286. https://doi.org/10.1111/trf.12079

Khan, S., P, M. R., Rizvi, A., Alam, M. M., Rizvi, M., & Naseem, I. (2019). ROS mediated antibacterial activity of photoilluminated riboflavin: A photodynamic mechanism against nosocomial infections. *Toxicology Reports*, *6*(October 2018), 136–142. https://doi.org/10.1016/j.toxrep.2019.01.003

Khodadadi, H., Zomorodian, K., Nouraei, H., Zareshahrabadi, Z., Barzegar, S., Zare, M. R., & Pakshir, K. (2021). Prevalence of superficial-cutaneous fungal infections in Shiraz, Iran: A five-year retrospective study (2015–2019). *Journal of Clinical Laboratory Analysis*, *35*(7), e23850. https://doi.org/https://doi.org/10.1002/jcla.23850

Kim, Y. J., Lee, H. I., Kim, J. K., Kim, C. H., & Kim, Y. J. (2020). Peptide 18-4/chlorin e6-conjugated polyhedral oligomeric silsesquioxane nanoparticles for targeted photodynamic therapy of breast cancer. *Colloids and Surfaces. B, Biointerfaces*, *189*, 110829. https://doi.org/10.1016/j.colsurfb.2020.110829

Kingsley, D. H., Perez-Perez, R. E., Boyd, G., Sites, J., & Niemira, B. A. (2018). Evaluation of 405-nm monochromatic light for inactivation of Tulane virus on blueberry surfaces. *Journal of Applied Microbiology*, *124*(4), 1017–1022.

https://doi.org/10.1111/jam.13638
Kubin, A., Wierrani, F., Burner, U., Alth, G., & Grünberger, W. (2005). Hypericin--the facts about a controversial agent. *Current Pharmaceutical Design*, *11*(2), 233–253. https://doi.org/10.2174/1381612053382287
Kunt, Z., Yağmur, M., Kandemir, H., Harbiyeli, I., Erdem, E., Kalkancı, A., De Hoog, G. S., & Ilkit, M. (2020). In Vitro Efficacy of Chlorhexidine and a riboflavin/UVA Combination on Fungal Agents of Keratitis. *Current Eye Research*, *45*(1), 7–11. https://doi.org/10.1080/02713683.2019.1652916
Li, H., Handsaker, B., Wysoker, A., Fennell, T., Ruan, J., Homer, N., Marth, G., Abecasis, G., & Durbin, R. (2009). The Sequence Alignment/Map format and SAMtools. *Bioinformatics (Oxford, England)*, *25*(16), 2078–2079. https://doi.org/10.1093/bioinformatics/btp352
Li, J., Lockerbie, O., de Korte, D., Rice, J., McLean, R., & Goodrich, R. P. (2005). Evaluation of platelet mitochondria integrity after treatment with Mirasol pathogen reduction technology. *Transfusion*, *45*(6), 920–926. https://doi.org/10.1111/j.1537-2995.2005.04381.x
Li, T., Zhao, Y., Matthews, K., Gao, J., Hao, J., Wang, S., Han, J., & Jia, Y. (2020). Antibacterial activity against Staphylococcus aureus of curcumin-loaded chitosan spray coupled with photodynamic treatment. *LWT*, *134*, 110073. https://doi.org/https://doi.org/10.1016/j.lwt.2020.110073
Liu, F., Li, Z., Cao, B., Wu, J., Wang, Y., Xue, Y., Xu, J., Xue, C., & Tang, Q. J. (2016). The effect of a novel photodynamic activation method mediated by curcumin on oyster shelf life and quality. *Food Research International*, *87*, 204–210. https://doi.org/10.1016/j.foodres.2016.07.012
López-Carballo, G., Hernández-Muñoz, P., Gavara, R., & Ocio, M. J. (2008). Photoactivated chlorophyllin-based gelatin films and coatings to prevent microbial contamination of food products. *International Journal of Food Microbiology*, *126*(1), 65–70. https://doi.org/10.1016/j.ijfoodmicro.2008.05.002
Luke-Marshall, N. R., Hansen, L. A., Shafirstein, G., & Campagnari, A. A. (2020). Antimicrobial Photodynamic Therapy with Chlorin e6 Is Bactericidal against Biofilms of the Primary Human Otopathogens. *MSphere*, *5*(4), 1–11. https://doi.org/10.1128/msphere.00492-20
Luksiene, Z., & Paskeviciute, E. (2011). Novel approach to the microbial decontamination of strawberries: Chlorophyllin-based photosensitization. *Journal of Applied Microbiology*, *110*(5), 1274–1283. https://doi.org/10.1111/j.1365-2672.2011.04986.x
Luksiene, Zivile. (2021). *Photosensitization: Principles and Applications in Food Processing* (pp. 368–384). https://doi.org/10.1016/B978-0-08-100596-5.22668-1
Luksiene, Zivile, & Paskeviciute, E. (2011). Microbial control of food-related surfaces: Na-Chlorophyllin-based photosensitization. *Journal of Photochemistry and Photobiology B: Biology*, *105*(1), 69–74. https://doi.org/10.1016/j.jphotobiol.2011.06.011
Mahdi, Z., Habiboallh, G., Mahbobeh, N. N., Mina, Z. J., Majid, Z., & Nooshin, A. (2015). Lethal effect of blue light-activated hydrogen peroxide, curcumin and erythrosine as potential oral photosensitizers on the viability of Porphyromonas gingivalis and Fusobacterium nucleatum. *Laser Therapy*, *24*(2), 103–111. https://doi.org/10.5978/islsm.15-OR-09
Makdoumi, K., Hedin, M., & Bäckman, A. (2019). Different photodynamic effects of blue light with and without riboflavin on methicillin-resistant Staphylococcus aureus (MRSA) and human keratinocytes in vitro. *Lasers in Medical Science*, *34*(9), 1799–1805. https://doi.org/10.1007/s10103-019-02774-9
Makuch, S., Dróżdż, M., Makarec, A., Ziółkowski, P., & Woźniak, M. (2022). An Update on Photodynamic Therapy of Psoriasis—Current Strategies and Nanotechnology as a Future Perspective. *International Journal of Molecular Sciences*, *23*(17). https://doi.org/10.3390/ijms23179845
Martins, S. A. R., Combs, J. C., Noguera, G., Camacho, W., Wittmann, P., Walther, R.,

Cano, M., Dick, J., & Behrens, A. (2008). Antimicrobial efficacy of riboflavin/UVA combination (365 nm) in vitro for bacterial and fungal isolates: A potential new treatment for infectious keratitis. *Investigative Ophthalmology and Visual Science*, *49*(8), 3402–3408. https://doi.org/10.1167/iovs.07-1592

Mattia, D. D., & Manikonda, K. (2018). Morbidity and Mortality Weekly Report Surveillance for Foodborne Disease Outbreaks — United States Centers for Disease Control and Prevention MMWR Editorial and Production Staff MMWR Editorial Board. *Surveillance Summaries MMWR*, *6262*(2), 1–11.

Mima, E. G., Vergani, C. E., Machado, A. L., Massucato, E. M. S., Colombo, A. L., Bagnato, V. S., & Pavarina, A. C. (2012). Comparison of Photodynamic Therapy versus conventional antifungal therapy for the treatment of denture stomatitis: a randomized clinical trial. *Clinical Microbiology and Infection : The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases*, *18*(10), E380-8. https://doi.org/10.1111/j.1469-0691.2012.03933.x

Mirshafiee, H., Sharifi, Z., Hosseini, S. M., Yari, F., Nikbakht, H., & Latifi, H. (2015). The effects of ultraviolet light and riboflavin on inactivation of viruses and the quality of platelet concentrates at laboratory scale. *Avicenna Journal of Medical Biotechnology*, *7*(2), 57–63.

Murray, C. J., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., Han, C., Bisignano, C., Rao, P., Wool, E., Johnson, S. C., Browne, A. J., Chipeta, M. G., Fell, F., Hackett, S., Haines-Woodhouse, G., Kashef Hamadani, B. H., Kumaran, E. A. P., McManigal, B., … Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*, *399*(10325), 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

Mytych, W., Bartusik-Aebisher, D., Łoś, A., Dynarowicz, K., Myśliwiec, A., & Aebisher, D. (2024). Photodynamic Therapy for Atherosclerosis. *International Journal of Molecular Sciences*, *25*(4). https://doi.org/10.3390/ijms25041958

Najafi, S., Khayamzadeh, M., Paknejad, M., Poursepanj, G., Kharazi Fard, M. J., & Bahador, A. (2016). An In Vitro Comparison of Antimicrobial Effects of Curcumin-Based Photodynamic Therapy and Chlorhexidine, on Aggregatibacter actinomycetemcomitans. *Journal of Lasers in Medical Sciences*, *7*(1), 21–25. https://doi.org/10.15171/jlms.2016.05

Najari, E., Zamani, S., Sheikh Arabi, M., & Ardebili, A. (2024). Antimicrobial photodynamic effect of the photosensitizer riboflavin, alone and in combination with colistin, against pandrug-resistant Pseudomonas aeruginosa clinical isolates. *Journal of Infection and Chemotherapy*, *July 2023*. https://doi.org/10.1016/j.jiac.2024.03.001

Nesi-Reis, V., Lera-Nonose, D. S. S. L., Oyama, J., Silva-Lalucci, M. P. P., Demarchi, I. G., Aristides, S. M. A., Teixeira, J. J. V., Silveira, T. G. V., & Lonardoni, M. V. C. (2018). Contribution of photodynamic therapy in wound healing: A systematic review. *Photodiagnosis and Photodynamic Therapy*, *21*, 294–305. https://doi.org/10.1016/j.pdpdt.2017.12.015

Nie, M., Deng, D. M., Wu, Y., de Oliveira, K. T., Bagnato, V. S., Crielaard, W., & Rastelli, A. N. de S. (2020). Photodynamic inactivation mediated by methylene blue or chlorin e6 against Streptococcus mutans biofilm. *Photodiagnosis and Photodynamic Therapy*, *31*(May), 101817. https://doi.org/10.1016/j.pdpdt.2020.101817

Nielsen, H. K., Garcia, J., Væth, M., & Schlafer, S. (2015a). Comparison of Riboflavin and Toluidine Blue O as Photosensitizers for Photoactivated Disinfection on Endodontic and Periodontal Pathogens In Vitro. *PloS One*, *10*(10), e0140720. https://doi.org/10.1371/journal.pone.0140720

Nielsen, H. K., Garcia, J., Væth, M., & Schlafer, S. (2015b). Comparison of riboflavin and toluidine blue O as photosensitizers for photoactivated disinfection on endodontic and periodontal pathogens in vitro. *PLoS ONE*, *10*(10), 1–11. https://doi.org/10.1371/journal.pone.0140720

Nigat, T. D., Sitote, T. M., & Gedefaw, B. M. (2023). Fungal Skin Disease Classification

Using the Convolutional Neural Network. *Journal of Healthcare Engineering*, *2023*. https://doi.org/10.1155/2023/6370416

Olaniran, A., Afolabi, R. O., Abu, H. E., Owolabi, A., Yetunde, I., Okolie, C., & Akpor, O. (2020). Lime potentials as biopreservative as alternative to chemical preservatives in pineapple, orange and watermelon juice blend. *Food Research*, *4*, 1878–1884. https://doi.org/10.26656/fr.2017.4(6).057

Oliveira, E. F., Tikekar, R., & Nitin, N. (2018). Combination of aerosolized curcumin and UV-A light for the inactivation of bacteria on fresh produce surfaces. *Food Research International (Ottawa, Ont.)*, *114*, 133–139. https://doi.org/10.1016/j.foodres.2018.07.054

Osuchowski, M., Bartusik-Aebisher, D., Osuchowski, F., & Aebisher, D. (2021). Photodynamic therapy for prostate cancer - A narrative review. *Photodiagnosis and Photodynamic Therapy*, *33*, 102158. https://doi.org/10.1016/j.pdpdt.2020.102158

Park, D., Kim, M., Choi, J. W., Baek, J.-H., Lee, S. H., & Baek, K. (2020). Antimicrobial photodynamic therapy efficacy against specific pathogenic periodontitis bacterial species. *Photodiagnosis and Photodynamic Therapy*, *30*, 101688. https://doi.org/10.1016/j.pdpdt.2020.101688

Paskeviciute, E., Zudyte, B., & Luksiene, Z. (2018). Towards better microbial safety of fresh produce: Chlorophyllin-based photosensitization for microbial control of foodborne pathogens on cherry tomatoes. *Journal of Photochemistry and Photobiology B: Biology*, *182*, 130–136. https://doi.org/10.1016/j.jphotobiol.2018.04.009

Paz-Cristobal, M. P., Gilaberte, Y., Alejandre, C., Pardo, J., Revillo, M. J., & Rezusta, A. (2014). In vitro fungicidal photodynamic effect of hypericin on Trichophyton spp. *Mycopathologia*, *178*(3–4), 221–225. https://doi.org/10.1007/s11046-014-9797-6

Pérez-Laguna, V., García-Luque, I., Ballesta, S., Rezusta, A., & Gilaberte, Y. (2021). Photodynamic Therapy Combined with Antibiotics or Antifungals against Microorganisms That Cause Skin and Soft Tissue Infections: A Planktonic and Biofilm Approach to Overcome Resistances. *Pharmaceuticals (Basel, Switzerland)*, *14*(7). https://doi.org/10.3390/ph14070603

Pérez-Laguna, V., García-Malinis, A. J., Aspiroz, C., Rezusta, A., & Gilaberte, Y. (2018). Antimicrobial effects of photodynamic therapy. *Giornale Italiano Di Dermatologia e Venereologia : Organo Ufficiale, Societa Italiana Di Dermatologia e Sifilografia*, *153*(6), 833–846. https://doi.org/10.23736/S0392-0488.18.06007-8

Pourhajibagher, M., Parker, S., Chiniforush, N., & Bahador, A. (2019). Photoexcitation triggering via semiconductor Graphene Quantum Dots by photochemical doping with Curcumin versus perio-pathogens mixed biofilms. *Photodiagnosis and Photodynamic Therapy*, *28*, 125–131. https://doi.org/https://doi.org/10.1016/j.pdpdt.2019.08.025

Praena, B., Mascaraque, M., Andreu, S., Bello-Morales, R., Abarca-Lachen, E., Rapozzi, V., Gilaberte, Y., González, S., López-Guerrero, J. A., & Juarranz, Á. (2022). Potent Virucidal Activity In Vitro of Photodynamic Therapy with Hypericum Extract as Photosensitizer and White Light against Human Coronavirus HCoV-229E. *Pharmaceutics*, *14*(11). https://doi.org/10.3390/pharmaceutics14112364

Pucelik, B., & Dąbrowski, J. M. (2022). Photodynamic inactivation (PDI) as a promising alternative to current pharmaceuticals for the treatment of resistant microorganisms. *Advances in Inorganic Chemistry*, *79*, 65–103. https://doi.org/10.1016/bs.adioch.2021.12.003

Rao, P. J., & Khanum, H. (2016). A green chemistry approach for nanoencapsulation of bioactive compound – Curcumin. *LWT - Food Science and Technology*, *65*, 695–702. https://doi.org/10.1016/j.lwt.2015.08.070

Rawson, K. A., & Dunlosky, J. (2011). Optimizing schedules of retrieval practice for durable and efficient learning: how much is enough? *Journal of Experimental Psychology. General*, *140*(3), 283–302. https://doi.org/10.1037/a0023956

Reddy, H. L., Dayan, A. D., Cavagnaro, J., Gad, S., Li, J., & Goodrich, R. P. (2008). Toxicity Testing of a Novel Riboflavin-Based Technology for Pathogen Reduction and

White Blood Cell Inactivation. *Transfusion Medicine Reviews*, *22*(2), 133–153. https://doi.org/10.1016/j.tmrv.2007.12.003

Rentas, F., Harman, R., Gomez, C., Salata, J., Childs, J., Silva, T., Lippert, L., Montgomery, J., Richards, A., Chan, C., Jiang, J., Reddy, H., Li, J., & Goodrich, R. (2007). Inactivation of Orientia tsutsugamushi in red blood cells, plasma, and platelets with riboflavin and light, as demonstrated in an animal model. *Transfusion*, *47*(2), 240–247. https://doi.org/10.1111/j.1537-2995.2007.01094.x

Saini, R., Marawar, P. P., Shete, S., & Saini, S. (2009). Periodontitis, a true infection. *Journal of Global Infectious Diseases*, *1*(2), 149–150. https://doi.org/10.4103/0974-777X.56251

Saitawee, D., Teerakapong, A., Morales, N. P., Jitprasertwong, P., & Hormdee, D. (2018). Photodynamic therapy of Curcuma longa extract stimulated with blue light against Aggregatibacter actinomycetemcomitans. *Photodiagnosis and Photodynamic Therapy*, *22*, 101–105. https://doi.org/10.1016/j.pdpdt.2018.03.001

Santos, R. F., Campos, B. S., Rego Filho, F. de A. M. G., Moraes, J. de O., Albuquerque, A. L. I., da Silva, M. C. D., dos Santos, P. V., & de Araujo, M. T. (2019). Photodynamic inactivation of S. aureus with a water-soluble curcumin salt and an application to cheese decontamination. *Photochemical & Photobiological Sciences*, *18*(11), 2707–2716. https://doi.org/10.1039/C9PP00196D

Schrier, A., Greebel, G., Attia, H., Trokel, S., & Smith, E. F. (2009). In vitro antimicrobial efficacy of riboflavin and ultraviolet light on Staphylococcus aureus, methicillin-resistant Staphylococcus aureus, and Pseudomonas aeruginosa. *Journal of Refractive Surgery (Thorofare, N.J. : 1995)*, *25*(9), S799-802. https://doi.org/10.3928/1081597X-20090813-07

Shen, S., Feng, J., Song, X., & Xiang, W. (2022). Efficacy of photodynamic therapy for warts induced by human papilloma virus infection: A systematic review and meta-analysis. *Photodiagnosis and Photodynamic Therapy*, *39*, 102913. https://doi.org/10.1016/j.pdpdt.2022.102913

Sheng, L., Li, X., & Wang, L. (2022). Photodynamic inactivation in food systems: A review of its application, mechanisms, and future perspective. *Trends in Food Science and Technology*, *124*(February), 167–181. https://doi.org/10.1016/j.tifs.2022.04.001

Sheng, L., & Wang, L. (2021). The microbial safety of fish and fish products: Recent advances in understanding its significance, contamination sources, and control strategies. *Comprehensive Reviews in Food Science and Food Safety*, *20*(1), 738–786. https://doi.org/10.1111/1541-4337.12671

Shin, J., Berg, D. A., Zhu, Y., Shin, J. Y., Song, J., Bonaguidi, M. A., Enikolopov, G., Nauen, D. W., Christian, K. M., Ming, G., & Song, H. (2015). Single-Cell RNA-Seq with Waterfall Reveals Molecular Cascades underlying Adult Neurogenesis. *Cell Stem Cell*, *17*(3), 360–372. https://doi.org/10.1016/j.stem.2015.07.013

Song, L., Zhang, F., Yu, J., Wei, C., Han, Q., & Meng, X. (2020). Antifungal effect and possible mechanism of curcumin mediated photodynamic technology against Penicillium expansum. *Postharvest Biology and Technology*, *167*(December 2019), 111234. https://doi.org/10.1016/j.postharvbio.2020.111234

Sperandio, F. F., Huang, Y.-Y., & Hamblin, M. R. (2013). Antimicrobial photodynamic therapy to kill Gram-negative bacteria. *Recent Patents on Anti-Infective Drug Discovery*, *8*(2), 108–120. https://doi.org/10.2174/1574891x113089990012

Stender, J., Pascual, G., Liu, W., Kaikkonen, M., Do, K., Spann, N., Boutros, M., Perrimon, N., Rosenfeld, M., & Glass, C. (2012). Control of Pro-Inflammatory Gene Programs by Regulated Trimethylation and Demethylation of Histone H4K20. *Molecular Cell*, *48*, 28–38. https://doi.org/10.1016/j.molcel.2012.07.020

Sun, D., Pang, X., Cheng, Y., Ming, J., Xiang, S., Zhang, C., Lv, P., Chu, C., Chen, X., Liu, G., & Zheng, N. (2020). Ultrasound-Switchable Nanozyme Augments Sonodynamic Therapy against Multidrug-Resistant Bacterial Infection. *ACS Nano*, *14*(2), 2063–2076. https://doi.org/10.1021/acsnano.9b08667

Svyatchenko, V. A., Nikonov, S. D., Mayorov, A. P., Gelfond, M. L., & Loktev, V. B. (2021). Antiviral photodynamic therapy: Inactivation and inhibition of SARS-CoV-2 in vitro using methylene blue and Radachlorin. *Photodiagnosis and Photodynamic Therapy*, *33*, 102112. https://doi.org/10.1016/j.pdpdt.2020.102112

Tao, R., Zhang, F., Tang, Q. juan, Xu, C. shan, Ni, Z. J., & Meng, X. hong. (2019). Effects of curcumin-based photodynamic treatment on the storage quality of fresh-cut apples. *Food Chemistry*, *274*, 415–421. https://doi.org/10.1016/j.foodchem.2018.08.042

Tonnetti, L., Thorp, A. M., Reddy, H. L., Keil, S. D., Goodrich, R. P., & Leiby, D. A. (2013). Riboflavin and ultraviolet light reduce the infectivity of Babesia microti in whole blood. *Transfusion*, *53*(4), 860–867. https://doi.org/10.1111/j.1537-2995.2012.03791.x

Torrungruang, K., Jitpakdeebordin, S., Charatkulangkun, O., & Gleebbua, Y. (2015). Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Treponema denticola / Prevotella intermedia Co-Infection Are Associated with Severe Periodontitis in a Thai Population. *PloS One*, *10*(8), e0136646. https://doi.org/10.1371/journal.pone.0136646

Tortik, N., Spaeth, A., & Plaetzer, K. (2014). Photodynamic decontamination of foodstuff from Staphylococcus aureus based on novel formulations of curcumin. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *13*(10), 1402–1409. https://doi.org/10.1039/c4pp00123k

Tosa, M., & Ogawa, R. (2020). Photodynamic therapy for keloids and hypertrophic scars: a review. *Scars, Burns & Healing*, *6*, 205951312093205. https://doi.org/10.1177/2059513120932059

Tosati, J. V, de Oliveira, E. F., Oliveira, J. V., Nitin, N., & Monteiro, A. R. (2018). Light-activated antimicrobial activity of turmeric residue edible coatings against cross-contamination of Listeria innocua on sausages. *Food Control*, *84*, 177–185. https://doi.org/10.1016/j.foodcont.2017.07.026

Tusi, J. S., Dyah, S., & Zaidan, A. H. (2015). Cahaya Led Biru Untuk Penyembuhan Luka Infeksi Secara in Vivo. *Biosains Pascasarjana*, *17*(3), 1–9.

Valle, C. A., Pérez-Laguna, V., Resta, I. M., Gavara, R., Felip-León, C., Miravet, J. F., Rezusta, A., & Galindo, F. (2020). A cost-effective combination of Rose Bengal and off-the-shelf cationic polystyrene for the photodynamic inactivation of Pseudomonas aeruginosa. *Materials Science and Engineering: C*, *117*, 111302. https://doi.org/10.1016/j.msec.2020.111302

Vallejo, M. C. S., Moura, N. M. M., Gomes, A. T. P. C., Joaquinito, A. S. M., Faustino, M. A. F., Almeida, A., Gonçalves, I., Serra, V. V., & Neves, M. G. P. M. S. (2021). The role of porphyrinoid photosensitizers for skin wound healing. *International Journal of Molecular Sciences*, *22*(8). https://doi.org/10.3390/ijms22084121

Verteporfirina, R. en la neovascularización corneal en pacientes tratados con terapia fotodinámica con, & Verteporfin, N. corneal regression in patients treated with photodynamic therapy with. (2016). Regresión en la neovascularización corneal en pacientes tratados con terapia fotodinámica con verteporfirina Neovascularization corneal regression in patients treated with photodynamic therapy with verteporfin. *Revista Médica Del Instituto Mexicano Del Seguro Social*, *54*(2), 164–169.

Vilas Boas, L. C. P., de Lima, L. M. P., Migliolo, L., Mendes, G. D. S., de Jesus, M. G., Franco, O. L., & Silva, P. A. (2017). Linear antimicrobial peptides with activity against herpes simplex virus 1 and Aichi virus. *Biopolymers*, *108*(2). https://doi.org/10.1002/bip.22871

Wang, D., Kyere, E., & Ahmed Sadiq, F. (2021). New Trends in Photodynamic Inactivation (PDI) Combating Biofilms in the Food Industry-A Review. *Foods (Basel, Switzerland)*, *10*(11). https://doi.org/10.3390/foods10112587

Wangsuwan, S., & Meephansan, J. (2019). Comparative Study Of Photodynamic Therapy With Riboflavin-Tryptophan Gel And 13% 5-Aminolevulinic Acid In The Treatment

Of Mild To Moderate Acne Vulgaris. *Clinical, Cosmetic and Investigational Dermatology*, *12*, 805–814. https://doi.org/10.2147/CCID.S227737

Warrier, A., Mazumder, N., Prabhu, S., Satyamoorthy, K., & Murali, T. S. (2021). Photodynamic therapy to control microbial biofilms. *Photodiagnosis and Photodynamic Therapy*, *33*, 102090. https://doi.org/10.1016/j.pdpdt.2020.102090

Willis, J. A., Cheburkanov, V., Kassab, G., Soares, J. M., Blanco, K. C., Bagnato, V. S., & Yakovlev, V. V. (2021). Photodynamic viral inactivation: Recent advances and potential applications. *Applied Physics Reviews*, *8*(2), 21315. https://doi.org/10.1063/5.0044713

Wu, J., Hou, W., Cao, B., Zuo, T., Xue, C., Leung, A. W., Xu, C., & Tang, Q. J. (2015). Virucidal efficacy of treatment with photodynamically activated curcumin on murine norovirus bio-accumulated in oysters. *Photodiagnosis and Photodynamic Therapy*, *12*(3), 385–392. https://doi.org/10.1016/j.pdpdt.2015.06.005

Wu, J., Mou, H., Xue, C., Leung, A. W., Xu, C., & Tang, Q. J. (2016). Photodynamic effect of curcumin on Vibrio parahaemolyticus. *Photodiagnosis and Photodynamic Therapy*, *15*, 34–39. https://doi.org/10.1016/j.pdpdt.2016.05.004

Xu, E., Xie, Y., & Al-Aly, Z. (2022). Long-term neurologic outcomes of COVID-19. *Nature Medicine*, *28*(11), 2406–2415. https://doi.org/10.1038/s41591-022-02001-z

Yow, C. M. N., Tang, H. M., Chu, E. S. M., & Huang, Z. (2012). Hypericin-mediated photodynamic antimicrobial effect on clinically isolated pathogens. *Photochemistry and Photobiology*, *88*(3), 626–632. https://doi.org/10.1111/j.1751-1097.2012.01085.x

Zago, L. H. de P., de Annunzio, S. R., de Oliveira, K. T., Barbugli, P. A., Valdes, B. R., Feres, M., & Fontana, C. R. (2020). Antimicrobial photodynamic therapy against metronidazole-resistant dental plaque bactéria. *Journal of Photochemistry and Photobiology B: Biology*, *209*, 111903. https://doi.org/10.1016/j.jphotobiol.2020.111903

Zhang, X., Wu, J., Xu, C., Lu, N., Gao, Y., Xue, Y., Li, Z., Xue, C., & Tang, Q. (2020). Inactivation of microbes on fruit surfaces using photodynamic therapy and its influence on the postharvest shelf-life of fruits. *Food Science and Technology International*, *26*(8), 696–705. https://doi.org/10.1177/1082013220921330

Žudytė, B., & Lukšienė, Ž. (2019). Toward better microbial safety of wheat sprouts: chlorophyllin-based photosensitization of seeds. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *18*(10), 2521–2530. https://doi.org/10.1039/c9pp00157c