Phytodynamic Therapy in Dental Perspective: A Review

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ABSTRACT:
Photodynamic therapy is an innovative technology that utilizes two non-toxic components, a photo-activating liquid and an LED light source to preferentially mark and destroy cariogenic bacteria and periodontal pathogens. The interaction between photosensitizer (PS) and light with adequate wavelength provides a wide effect spectrum. Photodynamic therapy (PDT), also known as photoactivated disinfection/ photochemotherapy/ photoradiation therapy/ phototherapy, has the potential to be a good alternative to the routine disinfection protocol.

Keywords- Photodynamic therapy, Phototsensitizer, Cytotoxic, Disinfection, Irradiation, Reactive Oxygen species.

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INTRODUCTION
Photoactivated disinfection (PAD) is based on the interaction of a photosensitive antibacterial agent and a light source. It uses a nontoxic dye (named photosensitizer PS) and low-intensity visible light. In oxygen presence, these combine to produce some cytotoxic species. The PS molecules attach to bacterial membrane. Photo-Activated Disinfection involves three components: light, a photosensitizer, and oxygen. A photosensitizer or its metabolic precursor is administered to the patient. Upon irradiation with light of a specific wavelength, the photosensitizer undergoes a transition from a low-energy ground state to an excited singlet state. Subsequently, the photosensitizer may decay back to its ground state, with emission of fluorescence, or may undergo a transition to a higher energy triplet state. The triplet state reacts with endogenous oxygen to produce singlet oxygen and other radical species, causing a rapid and selective destruction of the target tissue. Shrestha et. al. showed that antibacterial PDT with chitosan-conjugated rose Bengal nanoparticles can result in inactivation of LPS and subsequent reduction of all inflammatory markers. Various terms are used for PDT such as photoactivated chemotherapy (PACT), photodynamic disinfection (PDD), light-activated disinfection (LAD), and photoactivated disinfection (PAD) in different studies and literature. The success rate of photodynamic therapy depends on the type, dose, incubation time, and localization of the PS, the availability of oxygen, the wavelength of light (nm), the light power density and the light energy fluency.

History
The concept of treatment with light and photoactive compounds can be traced back over 6000 years to the ancient Egyptians who used light-sensitive substances (psoralens) by crushing leaves of plants related to parsley with sunlight to treat sunburns. Reference to the use of a plant extract for the restoration of skin pigmentation was made in 1400 BC and phototoxic effects of psoralens were described in 1250 AD. But the actual breakthrough came by Finsen’s pioneering research in 1901 in which he showed that skin tuberculosis could be successfully treated with natural and artificial ultraviolet light. The essential involvement of light and oxygen in the process was shortly thereafter demonstrated by Tappeiner, who coined the term ‘photodynamic’. Haxthausen and Hausmann in 1908 were the first to suggest that hematoporphyrin was a photodynamic photosensitizer. In 1960, Theodore Maiman, a scientist with the Hughes Aircraft Corporation, developed the first working laser device which emitted a deep red

**Mechanism of action**

Photosensitization is a treatment that involves the interaction of two non-toxic factors, such as a photo-active compound (tononium chloride) and a directly applied visible light (LED illumination at 635nm). Photo-Activated Disinfection requires a source of light that activates the photosensitizer by exposure to low-power visible light at a specific wavelength.

The light source for PAD can be divided into three main categories namely: 9

1) broad spectrum lamps,
2) Light emitting diode lamps (LED) and
3) lasers.

Most photosensitizers are activated by red light between 630 and 700 nm, corresponding to a light penetration depth from 0.5 cm (at 630 nm) to 1.5 cm (at ~ 700 nm). The ideal characteristics of a PS include:

1) Chemical purity & non-toxic.
2) Ability to target the tissue, cost-effective, easily available.
3) Short interval between administration of the drug and peak accumulation in the tissue.
4) Short half-life.
5) Activation at wavelength at which penetration into the target tissue is very good.
6) Ability to produce a large amount of cytotoxic products.

The most common PSs are phenothiazine, cyanine, phytotherapeutic agents, hematoporphyrin derivatives and xanthene derivatives. Phenothiazine dyes have been claimed to have intense absorption in 620 - 660 nm wavelength and so be useful in PDT. According to Chan and Lai, methylene blue shows maximal absorbance when exposed to a wavelength of 660 nm. Soares et. al. and Fernandes et. al. showed that toluidine blue O was preferred as a PS because it can easily pass through cell membrane. The transfer of electrons in activated PS can be done in two pathways including transfer to the neighboring molecule (type-1 reaction) or to oxygen (type-2 reaction) to produce reactive oxygen species (ROS), typically singlet oxygen. Although, the two pathways can have a role on bacterial killing, type 2 by producing highly reactive singlet oxygen is detected as the main pathway in killing bacteria.

Two mechanisms have a major role in lethal damage administered by PDT:

1) DNA damage,
2) Damage to cytoplasmic membrane and cellular contents or inactivation of membrane transport systems and enzymes.

Bacterial cells are typically composed of a variety of cytoplasmic materials enclosed by a cell wall. Many "traditional" anti-microbial substances must enter and accumulate inside the bacterium in order to destroy their targets. Since this process requires a transport mechanism through the cell wall, it gives the bacteria an opportunity to build up a resistance by modifying the transport mechanism required by the drug. This also applies to photo-activated drugs that must accumulate within the cell. Certain photoactive agents are taken up by bacteria preferentially, with the agent residing in the proximity of or becoming attached to the cell wall. Some may even enter microorganisms. All bacteria have the potential to be targeted, though some combinations between certain sensitizers and certain organisms are more successful than others. Healthy human tissue will not be affected. PAD techniques, use low power lasers to elicit a photochemical reaction in a photosensitizer, which in turn exerts a lethal effect on particular cells such as bacteria. PAD is basically a lethal laser photosensitization. Photosensitizers alone in the right doses are not toxic to bacteria. Low power (diode) laser energy in itself is, again, not particularly lethal to bacteria but is useful for photochemical activation of oxygen-releasing dyes. Singlet oxygen, a protoplastic poison released from dyes, causes lethal membrane, organ and DNA damage to microorganisms.

**Applications in dentistry**

Photodynamic therapy has also been used to disinfect carious dentin before restoration, disinfecting oral tissues before or during surgical procedures, treating denture stomatitis, and treating oral candidiasis in immune-compromised patients.

**Endodontic treatment**

Photodynamic therapy can be used in combination with mechanical instrumentation and chemical antimicrobial agents, such as NaOCl and hydrogen peroxide. Garcezet et. al. showed that endodontic treatment alone reduced 90% of bacteria, whereas PDT alone reduced it by 95%, the combination of these two techniques reduced bacteria by 98%. PDT has shown to be effective against Gram positive as well as Gram-negative endodontic pathogens like Enterococcus faecalis, Streptococcus intermedius, Fusobacterium nucleatum, Pepto streptococcus micros, Prevotella intermedia. Garcezet et. al. demonstrated that usage of PDT added to endodontic treatment of infected canals with the optical fiber may be better than when the laser is used directed at the cavity. In a case report, Johns et. al. described a new protocol for pulp revascularization with canal disinfection using a combination of a low-power laser light and PS solution.
Effect on bond strength
An in vitro study evaluated the effect of the PAD system on the bond strength of AH Plus, Sealapex, and MTA Fillapex root canal sealers using the push-out test design. Findings revealed that AH Plus and MTA Fillapex sealers had greater bond strength compared with Sealapex root canal sealers. It was also revealed that the PAD system adversely affected the bond strength of the MTA Fillapex root canal sealer to dentin.

Dental Caries
With regard to bacteria involved in dental caries, Burns et al. showed that tolonium chloride (25 g/mL) used with 632.8 nm laser energy reduced the viability of Streptococcus mutans, Streptococcus sobrinus, Lactobacillus casei, and Actinomyces viscosus. The technique involves applying a photo-active solution that is absorbed selectively by cariogenic bacteria to the operative surfaces. This sensitizes them to the application of visible illumination which causes cytotoxic bacterial reactions that result in selective destruction of the target microorganism.

Periodontal therapy
Scaling and root planning can remove the calculus and plaque but has little effect on the acidogenic and aciduric bacteria that is the cause of these deposits and the ensuing periodontal disease that has been associated with numerous systemic health problems. Research has indicated that PAD mechanism functions to combat the bacteria that are largely responsible for periodontitis like porphyromonas gingivalis, Actinobacillus actinomycetem comitans, Fusobacterium nucleatum, Streptococcus sanguinis, Bacteroides forsythus, Campylobacter rectus and Eikenella corrodens.

Other applications of PAD
Photodynamic Antimicrobial Chemotherapy (PACT) represents an alternative antibacterial, antifungal and antiviral treatment for drug resistant micro-organisms. It is unlikely that bacteria would develop resistance to the cytotoxic action of singlet oxygen or free radicals. Applications of PAD are growing rapidly in the treatment of oral cancer, bacterial, fungal infections and diagnosis of malignant transformation. Limitations of this treatment which should be taken into account are the low-oxygenated environment and the diffusion ability of the PS and light to be used.

CONCLUSION
With Photodynamic therapy, the remaining tooth surfaces are disinfected and thus are far more likely to remineralize effectively. Photo-activated disinfection offers a heightened level of disinfection during and after operative and periodontal procedures. Despite being an effective auxiliary tool to antimicrobial therapy, further studies needed in order to determine appropriate parameters for photosensitizer concentration, energy dosage used, time of irradiation, and exposure.

REFERENCES:


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