

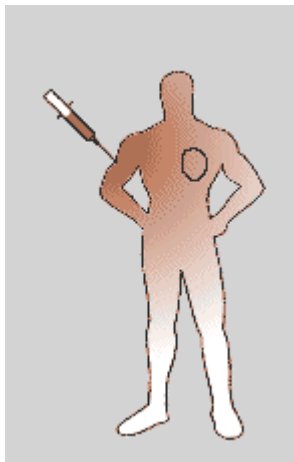
Photodynamic therapy (PDT)

Photodynamic therapy (PDT) is a special form of phototherapy, a term which includes all treatments which use light to induce reactions in the body which are of benefit to patients.

PDT is a developing technique which can potentially destroy unwanted tissue, whilst sparing normal tissue. Photodynamic action refers to the ability of certain compounds, called **photosensitisers**, to destroy or inhibit the growth of living cells when exposed to light. The photosensitiser is not consumed during the process and may therefore be regarded as a catalyst, or energy transfer agent, where its primary purpose is to capture and channel the energy of light into the biological processes leading to cell death. The correct choice of photosensitiser is critical if the photodynamic effect is to be truly beneficial, as it has to be readily deliverable to the relevant cells, either by systemic administration or topical application

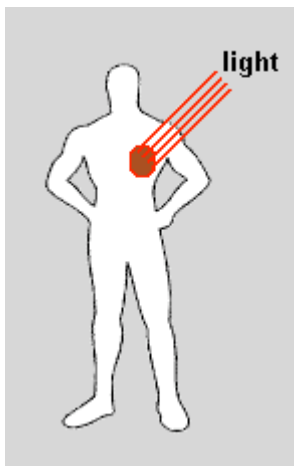
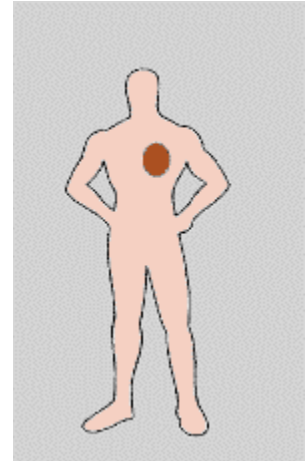
Some of the drugs being developed also have the desirable property of concentrating in tumours (and certain other kinds of proliferating tissue) relative to the surrounding healthy tissue, which also helps in targeting. There is only one potentially adverse effect - some drugs can result in skin photosensitivity, which means that patients must stay out of bright light for some time following the administration of the drug.

The way that PDT works in patients is shown below:



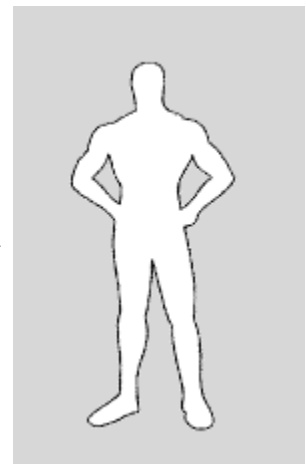
A patient comes to the clinic with a tumour.
The photosensitiser is given by injection.

After time the photosensitiser concentrates
in the tumour.



The photosensitiser is activated by light

The tumour is selectively destroyed



So from above diagrams, it is clear that essential component of PDT are photosensitisers, oxygen and light. Presence of all of them is necessary for successful PDT treatment. So properties of these components are:

Photosensitisers

The primary requirements of a photosensitiser are

- a) It should absorb light efficiently
- b) In the presence of oxygen it should be able to use the light energy to generate singlet oxygen efficiently.

To be of any therapeutic value, there are equally important secondary requirements, namely:

- The photosensitiser should have an absorption band in the 600-750 nm range, in order to ensure that the absorbed light (red or near-infrared) will readily penetrate cells, tissue and blood.
- It should have little or no host toxicity in the absence of light.
- It should rapidly clear from normal tissue (especially skin) so that there is no prolonged sensitivity to light after treatment.
- It should show some degree of preferential uptake by the target cells relative to the host tissue.

Current clinically used photosensitisers belong to the porphyrin-related molecular classes.

Light Sources

For effective PDT a light source is required with output over a specific wavelength range.

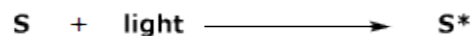
There are several types of light source that can be used for a photodynamic treatment including: broad spectrum halogen lamps, light emitting diodes (LEDs) and lasers (none of these light sources involve heating of tissue). The choice of

light source to use can depend on both the light dose required and also the geometry of the illumination area. Light source technology for PDT has advanced significantly over recent years leading to cheaper and more efficient products.

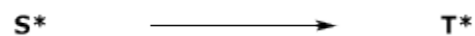
Theory

The photodynamic effect is based on the following sequence of events:

1. Absorption of light energy by the photosensitiser (S), so promoting it to a highly energetic singlet state, S*.



2. Efficient conversion of the energized S* singlet state of the photosensitiser into an energized triplet state T*.



3. Transfer of the energy from T* to normal molecular oxygen, O₂, to give highly activated oxygen (singlet oxygen).



In this process the original photosensitiser S is formed and is then available to be used again.

4. Destruction of a living cell by singlet oxygen attack.



Advantages of Photodynamic Therapy

1. Selectivity

Photodynamic therapy can provide distinct advantages over traditional methods for treating disease, and many of these stem from the unique selectivity or targeting ability of the technique. Thus it is possible to kill target cells (e.g. bacteria or cancer cells) whilst sparing normal body cells. This can be achieved because of the following:

- The activating light source can be precisely targeted to the treatment area.
- Singlet oxygen, the prime cytotoxic agent, has only a very short lifetime in a cellular environment, and consequently it can only harm the cell in which it is generated. This also means that once the light source is removed there is no further toxic effect.
- The rate at which a photosensitiser is taken up will be different for different cells and tissues. Thus it is possible to select a time interval between administering the photosensitiser and applying the light source that will optimize the preferential uptake of the photosensitiser by the target cells.

2. Broad spectrum activity

Singlet oxygen can kill any living cell providing

- (a) it is generated in sufficiently close proximity to vital cell components
- (b) it is generated in sufficiently high concentration.

As the first requirement is determined by the correct choice of photosensitiser, and the second by the intensity and duration of the light, in principle any microorganism (virus, bacterium, yeast, spore, parasite) can be destroyed by the photodynamic effect.

3. Low risk of acquired resistance by infective microorganisms

Unlike antibiotics and other conventional anti-infective agents, the photodynamic effect is multi-targeted as singlet oxygen attacks many cell sites and disrupts

many cell processes. Thus the likelihood of a microorganism mutating to protect itself against all such types of event is small.

References

1. Macdonald et. al. Basic principles of photodynamic therapy. ***J. Porphyrins and Phthalocyanines* 2001;5:105-129**
2. Dolmans et al. Photodynamic therapy for cancer. ***Nature* 2003;3: 380**
3. Website of University of Leeds Centre for Photobiology and Photodynamic Therapy (PDT).

<http://www.bmb.leeds.ac.uk/pdt>