

The characterisation of three substituted zinc phthalocyanines of differing charge for use in photodynamic therapy. A comparative study of their aggregation and photosensitising ability in relation to *m*THPC and polyhaematoporphyrin

Denise J. Ball^{a,*}, Simon R. Wood^a, David I. Vernon^a, John Griffiths^a,
Tom M.A. R. Dubbelman^b, Stanley B. Brown^a

^a Centre for Photobiology and Photodynamic Therapy, University of Leeds, Leeds LS2 9JT, UK

^b Molecular Cell Biology, Leiden University, Leiden, Netherlands

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Abstract

Three substituted zinc (II) phthalocyanines (one anionic, one cationic and one hydrophobic) have been compared to two clinically used photosensitisers, 5,10,15,20-tetra(*m*-hydroxyphenyl)chlorin (*m*THPC) and polyhaematoporphyrin (PHP), as potential agents for photodynamic therapy (PDT). Oxygen-consumption experiments, performed to follow the photo-oxidation of tryptophan, histidine and bovine serum albumin (BSA), suggest that the anionic phthalocyanine is the most efficient photosensitiser. The efficacy of BSA oxidation is much greater than that of tryptophan or histidine, which is partly due to monomerisation of the sensitisers upon binding to BSA. Spectra recorded in aqueous solution reveal that all five compounds are highly aggregated, but monomerisation is induced upon the addition of BSA or methanol. Using a range of methanol–buffer solutions, the aggregation state has been directly related to the efficacy of tryptophan photo-oxidation with maximal rates of oxidation achieved when the sensitiser is monomeric. Using erythrocytes as a simple membrane model, the efficacy of each sensitiser exhibits a different trend from that predicted by oxygen-consumption experiments. The anionic phthalocyanine is the least effective at photo-haemolysis, whereas the cationic and hydrophobic phthalocyanines have improved activity over PHP and *m*THPC. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Photodynamic therapy; Photosensitizers; Phthalocyanines

1. Introduction

Photodynamic therapy (PDT) is a developing cancer treatment involving the administration of a photosensitising compound and its subsequent activation by light [1]. The clinically used photosensitiser, Photofrin®, is a porphyrin preparation which has been approved for use in the USA, Canada, The Netherlands and Japan, proving effective for the treatment of bladder, lung, oesophagus, gastric and cervical cancers [2]. The corresponding photosensitiser used in our Centre is termed polyhaematoporphyrin (PHP) and is chemically identical to Photofrin as judged by high-purity liquid chromatography (HPLC) and chemical analysis [3].

Although porphyrin-mediated PDT has been successful on a wide range of neoplasms, it is not without its drawbacks,

such as low absorption in the red region of the spectrum and prolonged skin photosensitivity [4]. Attempts to circumvent some of the problems associated with the porphyrin-based compounds have been directed toward the development of so-called ‘second-generation’ photosensitisers [5], such as the chlorins [6–8] and phthalocyanines [9–12].

One of the most promising chlorins is 5,10,15,20-tetra(*m*-hydroxyphenyl)chlorin (*m*THPC, Foscan®) [13]. *m*THPC fulfils many of the requirements of a second-generation photosensitiser; it is a single, pure compound with a high absorption in the red ($\epsilon_{652} = 22\,000\text{ M}^{-1}\text{ cm}^{-1}$), selectivity for tumour tissue [14], and low concentrations ($0.75\ \mu\text{mol kg}^{-1}$) combined with low fluence rate (10 J cm^{-2}) have been shown to result in considerable depth of tumour necrosis ($> 5\text{ mm}$) [15]. In addition, a high rate of photobleaching has been observed both in vitro [16] and in vivo [17], which may reduce the risk of skin damage.

* Corresponding author. Fax: +44-113-233-3017; E-mail: bmbdjb@bmb.leeds.ac.uk

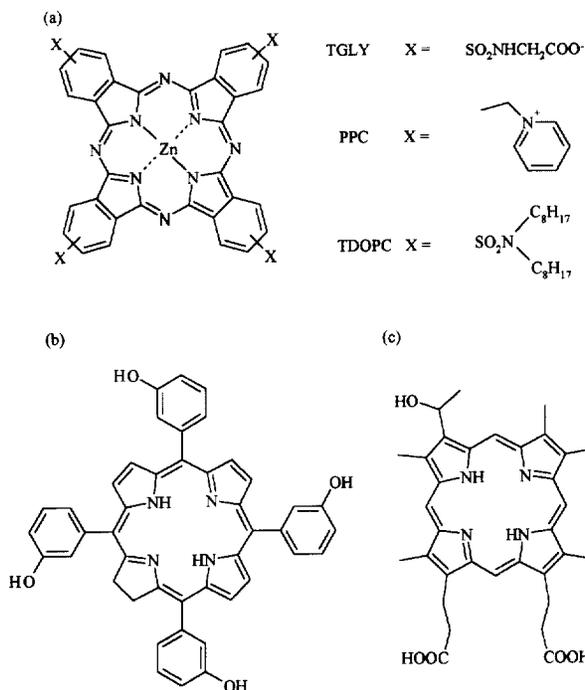


Fig. 1. Structures of (a) substituted zinc (II) phthalocyanines, (b) *m*THPC and (c) PHP.

Phthalocyanines (Pcs) are porphyrin-like synthetic compounds that have been used for many years as dyes in the textile industry [10]. They exhibit an increased *Q*-band extinction coefficient approximately 50 times higher than Haematoporphyrin Derivative (HpD) ($\epsilon_{600-700} \sim 10^5 \text{ M}^{-1} \text{ cm}^{-1}$) that is red shifted, allowing deeper light penetration [11]. The Pc macrocycle can be derivatised by metal chelation and peripheral substitution. Chelation with diamagnetic metals (e.g., zinc, aluminium) produces phthalocyanines with extended triplet lifetimes [18]. Substitution with hydrophilic groups results in the formation of stacked aggregates when dissolved in aqueous solution, restricting contact of the hydrophobic skeleton with water. The aggregated Pc is much less fluorescent and has reduced photosensitising ability [18]. Disaggregation of the stacked dye molecules can be achieved by the addition of organic solvent, detergents or serum proteins [19] and can be observed spectrophotometrically with a red shift in λ_{max} from approximately 630 to 680 nm [19].

We have developed zinc (II) phthalocyanine derivatives that differ in their overall charge and hydrophobicity [20] to allow comparisons of structure–function relationships. These have been shown to have good photodynamic activity *in vitro* and *in vivo* [21,22]. The aim of the current work was to determine the extent to which the aggregation state affects the photodynamic efficacy of three substituted zinc (II) phthalocyanines with comparisons to *m*THPC and PHP (Fig. 1). Oxygen-consumption experiments were performed with histidine (His), which has specificity for energy transfer (type II reactions), and with tryptophan (Trp), which is oxidised via electron- and energy-transfer reactions (mixed

type I/II reaction) [23]. Furthermore, because proteins are important targets of PDT [24], and because proteins induce monomerisation upon sensitizer binding [19], the photo-oxidation of bovine serum albumin (BSA) was also monitored. Photo-oxidation experiments performed in simple solution provide valuable information on structure–activity relationships, but neglect the effect of membrane interactions, therefore the photo-haemolysis of red blood cells was also used as a simple model system.

2. Methods

2.1. Photosensitisers

The three zinc (II) phthalocyanines, TGly, TDOPc and PPC were synthesised by Mr J. Schofield, Department of Colour Chemistry, Centre for Photobiology and Photodynamic Therapy, University of Leeds. TGly and TDOPc are tetrasubstituted (J. Schofield, personal communication), whilst PPC is reported to be primarily disubstituted [20]. PHP was supplied by Dr D.I. Vernon, School of Biochemistry and Molecular Biology, Centre for Photobiology and Photodynamic Therapy, at a concentration of 1 mg ml^{-1} in PBS, and stored at -20°C in working aliquots. *m*THPC (Foscan®) was kindly donated by Scotia Quanta Nova (Guilford, Surrey, UK) and solutions were freshly prepared each day according to the manufacturer's guidelines in PEG/ethanol/water (2:3:5 vol./vol.). Octanol/buffer partition experiments were performed to determine the hydrophobicity.

2.2. The effect of methanol concentration on the aggregation state of photosensitisers

Aggregation was studied spectrophotometrically over a range of methanol–buffer solutions (0–95%). Photosensitizer stock solutions were prepared at 2.5 mg ml^{-1} . Dilution of the sensitizer was achieved using the required methanol solution to give a final working concentration of $25 \mu\text{g ml}^{-1}$ (phthalocyanines) or $10 \mu\text{g ml}^{-1}$ (PHP and *m*THPC). All readings and solutions were at room temperature. The ratio of the absorbance values at the peak wavelengths was taken as an indication of aggregation state [25]. To confirm that the ratio of the spectral bands was not merely a solvatochromic effect, similar plots were performed as a function of sensitizer concentration in either phosphate buffer or 25% methanol by using cuvettes of different path length.

2.3. The effect of methanol concentration on the photo-oxidation of tryptophan

Sensitisers were prepared as 0.1 mM solutions. Tryptophan (Sigma, Dorset, UK) was dissolved in phosphate buffer to a concentration of 10 mM. Methanol solutions were prepared by dilution in phosphate buffer (pH 7.2) to achieve concentrations ranging from 10 to 90% methanol. A standard curve

of tryptophan fluorescence against concentration was produced and was linear over the relevant concentration range. Tryptophan (30 μl) was added to the different methanol solutions in the presence, or absence, of sensitiser (10 μM), to a final volume of 3 ml, in a sealed glass vial. The solution was then irradiated using white light from a 1000 W quartz halogen lamp (Ushio, Japan; Oriel, CT, USA), the light from which was focused through a glass tank containing water to prevent sample warming.

At 5 min time intervals, samples were removed and diluted with phosphate buffer (pH 7.2) in a quartz cuvette. The Trp fluorescence was recorded ($\lambda_{\text{ex}} = 280 \text{ nm}$, $\lambda_{\text{em}} = 350 \text{ nm}$) and the concentration of Trp at each time point was calculated by comparison with standards. The rate of Trp degradation was thus calculated over a 1 h time period. Plots of $\ln[\text{Trp}]$ versus time, for each concentration of methanol, were linear, and from these first-order rate constants, k , were determined, where $\text{Rate} = k[\text{Trp}]$. Under the conditions of the experiment there was no interference from sensitiser fluorescence, nor was there any degradation of Trp in the absence of sensitiser.

2.4. Oxygen-consumption measurements

Photosensitisers were prepared as 0.1 mM solutions in phosphate buffer (TGly, PPC, PHP), PEG/ethanol/water (*m*THPC) or isopropanol (TDOPc). Stock solutions of the photo-oxidisable substrates His (1 mM), Trp (1 mM) and BSA (1%) were prepared in 50 mM phosphate buffer (pH 7.2). Photosensitiser was added to a final concentration of 10 μM . The amount of oxygen consumption was determined using a YSI Biological Oxygen Monitor (model 5300, OH, USA) equipped with a Clark-type electrode. Red-light illumination was achieved using a slide projector (150 W xenophot HLX 64640 lamp) fitted with a red filter (band pass $> 600 \text{ nm}$, 46 mW cm^{-2}). Experiments were performed at room temperature and the oxygen concentration in the solution was 0.284 mM. This gave an electrode calibration value of 100%. Each sensitiser was tested in triplicate and the rate of oxygen consumption calculated as percentage decrease per minute.

2.5. Red blood cell haemolysis

Blood was collected in pooled buffy coats from the Regional Red Cross Blood Bank, Leidsenhage, The Netherlands. Erythrocytes were separated from leukocytes and plasma by centrifugation (2000g, 15 min) and washed three times in PBS (pH 7.4). A 2% erythrocyte suspension was then prepared by dilution in PBS.

Sensitiser was added to a final concentration of 10 μM to 5 ml erythrocyte suspension in a conical flask. The erythrocyte suspension was then irradiated (in the presence of sensitiser) with red light (46 mW cm^{-2}) using a slide projector and red filter. The irradiation was achieved through a glass water bath to avoid sample heating and the solution was

magnetically stirred throughout the duration of the experiment.

At appropriate time intervals, aliquots of erythrocyte suspension were removed, centrifuged (2000g, 10 s) to pellet the red blood cells, and the supernatant collected. Analysis of potassium ions (K^+) was performed using a Corning flame photometer (Corning 410C, UK) and haemoglobin (Hb) content was determined by absorbance at 540 nm.

For each experiment, 100% haemolysis was taken as the value obtained when aliquots of the erythrocyte suspension were placed directly in water. Experiments were performed in triplicate and the results expressed as the time taken for 50% K^+ or Hb release.

3. Results

3.1. Hydrophobicity

Octanol/buffer partition experiments were performed to determine the hydrophobicity. PPC and TGly were found exclusively in the buffer phase, TDOPc and *m*THPC were contained in the octanol layer and PHP was distributed equally between both layers at pH 7, resulting in a partition coefficient of zero.

3.2. Spectral properties of aggregation

The absorption spectra of all five compounds ($25 \mu\text{g ml}^{-1}$ phthalocyanines, $10 \mu\text{g ml}^{-1}$ of each PHP and *m*THPC) are shown in Fig. 2 and the corresponding peak wavelengths are outlined in Table 1. In neutral aqueous solution, the phthalocyanines display a typically aggregated spectrum which is characterised by two main peaks in the 600–700 nm region, at approximately 630 and 680 nm [10]. On the addition of organic solvent, spectral changes indicative of monomerisation occur, i.e., an increase in the absorption at 680 nm and the disappearance of the peak at 630 nm. For TGly and TDOPc this was also accompanied by the appearance of a new peak around 610 nm. However, even in 100% methanol the persistence of some aggregated species was suggested by the shoulder in the 630 nm region.

Like most porphyrins, *m*THPC, a chlorin-type photosensitiser, is prone to aggregation. The aggregated species is characterised by a broad Soret band with a λ_{max} of 436 nm [26]. On the addition of organic solvent there is a blue shift in λ_{max} to 416 nm with a concomitant increase in intensity, indicative of disaggregation [26].

In buffered water, PHP displays a typical porphyrin profile with a broad absorption peak in the Soret region (350–400 nm) and four smaller *Q* bands. The aggregated spectrum is characterised by a λ_{max} of 364 nm and a shoulder around 380 nm, suggestive of several species in different states of aggregation. On the addition of organic solvent, a red shift is observed ($\lambda_{\text{max}} = 388 \text{ nm}$) and hyperchromicity, indicative of monomerisation [25].

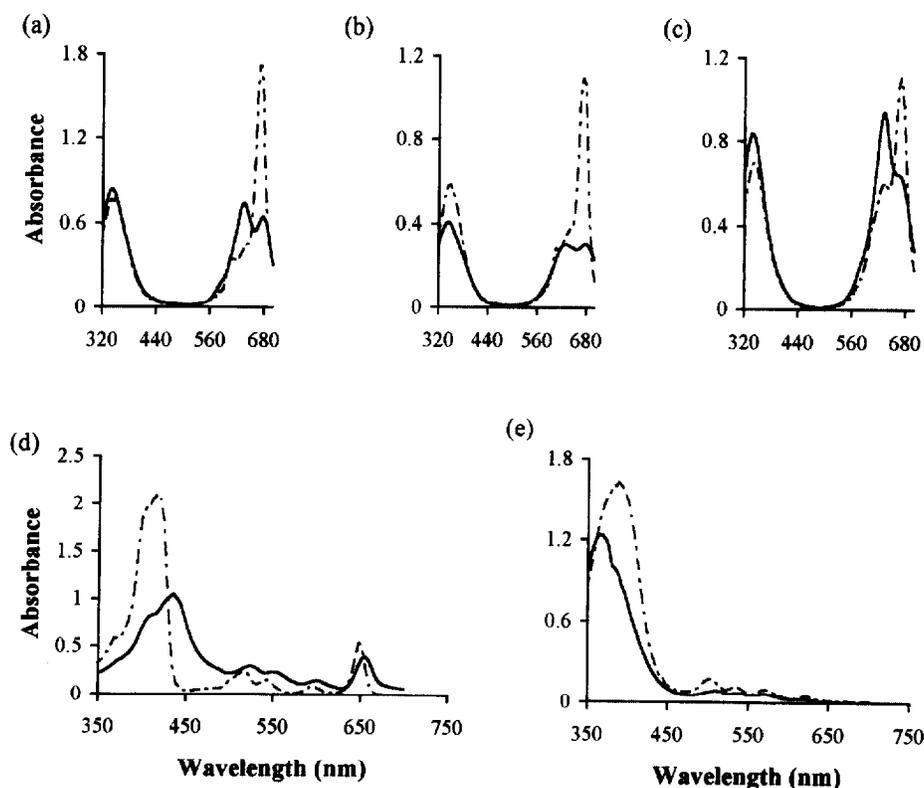


Fig. 2. Absorption spectra of (a) TGly ($25 \mu\text{g ml}^{-1}$), (b) TDOPc ($25 \mu\text{g ml}^{-1}$), (c) PPC ($25 \mu\text{g ml}^{-1}$), (d) *m*THPC ($10 \mu\text{g ml}^{-1}$) and (e) PHP ($10 \mu\text{g ml}^{-1}$) recorded in buffered water (—) and methanol (---).

Table 1

The absorption maxima of each sensitizer ($25 \mu\text{g ml}^{-1}$ phthalocyanines, $10 \mu\text{g ml}^{-1}$ *m*THPC and PHP) in buffered water and in methanol (for *m*THPC and PHP the wavelength maxima in the red region are also given for comparison)

Sensitizer	Concentration (μM)	λ_{max} (methanol) (nm)	λ_{max} (buffer) (nm)
TGly	18	672	636
TDOPc	14	672	632
PPC	25	668	632
<i>m</i> THPC	14.7	416 (652)	436 (656)
PHP	16.7	388 (626)	364 (632)

3.3. The effect of methanol concentration on sensitizer aggregation

The addition of methanol has been shown to have an effect on the aggregation state of PPC and PHP [27]. Absorption spectra were recorded in methanol–buffer mixtures at fixed sensitizer concentrations ($25 \mu\text{g ml}^{-1}$ phthalocyanines, $10 \mu\text{g ml}^{-1}$ *m*THPC and PHP). The changes in aggregation state were then observed graphically by a plot of methanol concentration against absorption peak ratios (Fig. 3) [25]. At a constant concentration of TGly, an increase in methanol concentration was accompanied by an increase in the ratio of the 630:680 nm peaks, reaching a maximum at 60–80% methanol. At methanol concentrations greater than 80% there was

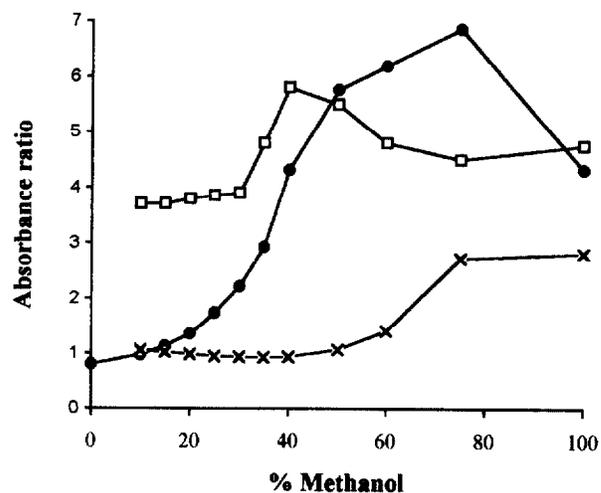


Fig. 3. The effect of methanol concentration on the aggregation state of TGly (●), TDOPc (×) and *m*THPC (□) as determined by the absorption ratio of the peak wavelengths.

a fall in peak ratio, possibly indicative of re-aggregation. Similar effects have been reported with PPC and PHP [27].

To confirm that this change in peak ratio was not merely a solvatochromic effect, absorbance spectra of TGly were recorded at a range of concentrations (0.5 – $50 \mu\text{g ml}^{-1}$) in phosphate buffer and in 25% methanol/phosphate buffer (Fig. 4). In pure phosphate buffer, there was no change in the absorbance spectra with an aggregated species present at all concentrations. However, in 25% methanol there was a

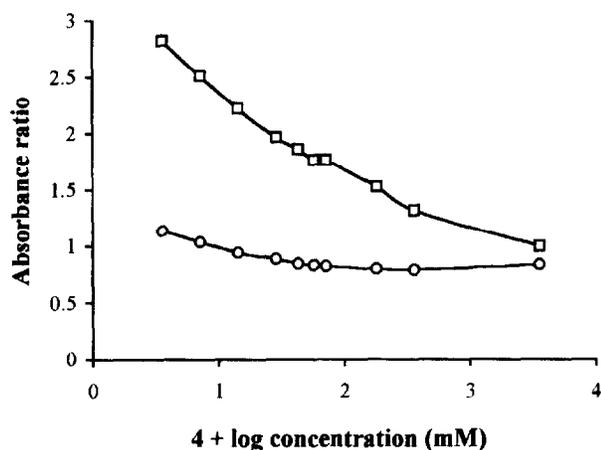


Fig. 4. The effect of decreasing concentration of TGly on the aggregation state in phosphate buffer (○) and 25% methanol (□) as determined by the ratio of the absorption at 674 nm to that at 632 nm.

marked change in the absorption spectra with an aggregated spectrum at high concentrations and a more monomeric spectrum predominating at low concentrations. This marked deviation from the Beer–Lambert law suggests the existence of more than one species of TGly in different states of aggregation. No single isosbestic point was observed, implying that this was more than a simple monomer–dimer equilibrium.

The hydrophobic phthalocyanine, TDOPc, did not show any changes in the absorption spectrum until the concentration of methanol present was greater than 60% (Fig. 3). In 100% methanol, *m*THPC gave a typical chlorin-type spectrum (Fig. 2). Addition of phosphate buffer resulted in spectral changes involving a broadening of the absorbance peaks and a concomitant decrease in extinction coefficient. A plot of the ratio of the Soret peak to the peak at 648 nm against methanol concentration shows that the absorption ratio was constant in the 0–30% methanol range, then rose to a peak in 55% methanol. Further additions of methanol were accompanied by a small decrease in the absorbance peak ratio.

3.4. Tryptophan photo-oxidation

To correlate photosensitising ability with aggregation state, first-order photo-oxidation rate constants, k , were obtained for a range of methanol concentrations (Fig. 5). TGly and *m*THPC gave a bell-shaped curve that increased to a peak, then declined upon further additions of methanol. Similar results have been shown for PPC and PHP [27]. Table 2 summarizes the maximal rate constant and corresponding methanol concentration for each sensitiser. TGly gave the best rate of tryptophan oxidation, which was maximal in 50% methanol. This is consistent with the changes observed in the aggregation state (Fig. 3). The remaining sensitisers were less efficient than the current clinically used photosensitiser (PHP), with the rate constant for TDOPc being one third that of PHP.

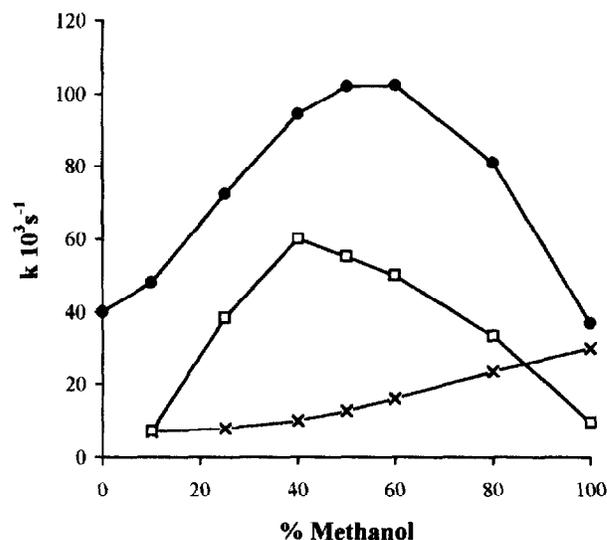


Fig. 5. The effect of methanol concentration on the first-order rate constant, k , for the photo-oxidation of trp by TGly (●), TDOPc (×) and *m*THPC (□).

Table 2

The maximal rate constant of each sensitiser and the corresponding methanol concentration in which the rate was maximal

Sensitiser	$k \ 10^3 \ s^{-1}$	% Methanol at peak rate
TGly	112	50
TDOPc	30	100
PPC	88.4 ^a	60 ^a
<i>m</i> THPC	61.7	40
PHP	95.2 ^a	40 ^a

^a Ref. [27].

3.5. Oxygen-consumption experiments

Table 3 summarizes the results of oxygen-consumption measurements recorded during the red-light illumination of equimolar concentrations of each sensitiser in the presence of Trp, His or BSA. TGly was the most efficient at photo-oxidation. PPC and PHP were approximately half as efficient as TGly, whilst TDOPc and *m*THPC gave negligible rates of oxidation of Trp and His. TDOPc and *m*THPC have a greater extinction coefficient in the red part of the spectrum than PHP

Table 3

Oxygen consumption during the photo-oxidation of tryptophan (1 mM), histidine (1 mM) and bovine serum albumin (1%) in 50 mM phosphate buffer (pH 7.2). Sensitiser was added to a final concentration of 10 μ M

Sensitiser	Oxygen consumption (% min ⁻¹)		
	Tryptophan	Histidine	BSA
TGly	5.6 ± 0.12	5.3 ± 0.14	56.3 ± 1.5
TDOPc	N.R.	N.R.	5.7 ± 0.8
PPC	2.81 ± 0.4	2.78 ± 0.03	21 ± 0.31
<i>m</i> THPC	N.R.	N.R.	2.8 ± 0.22
PHP	2.3 ± 0.06	2.8 ± 0.2	3.7 ± 0.3

N.R. = no oxygen consumption recorded over 30 min.

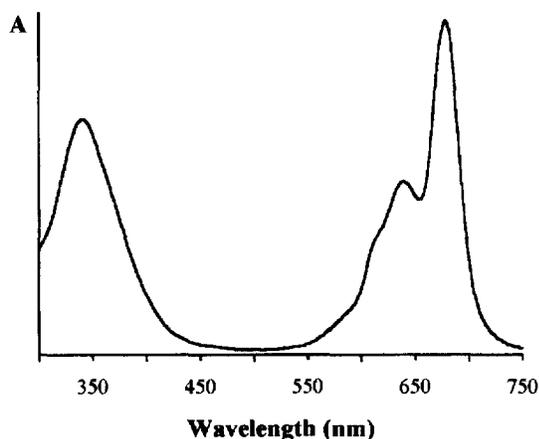


Fig. 6. The absorption spectrum of TGly (10 μ M) in 1% BSA.

(Fig. 2), therefore the poor rates of oxidation observed with these sensitiser probably reflect their highly hydrophobic and aggregated nature [28]. All five sensitiser were more efficient at oxidation of BSA than Trp or His. The monomerising effect of serum on photosensitiser is well recognised [19,24] and is exemplified by Fig. 6, which depicts a typically monomeric spectrum of TGly (10 μ M) in 1% BSA. Similar spectra were recorded for each sensitiser and these were comparable to the spectra recorded in methanol (Fig. 2). Therefore, the more efficient oxidation of BSA probably reflects the greater amount of monomeric, and hence photo-active, dye available.

3.6. Red blood cell haemolysis

Fig. 7 summarizes the results obtained when equimolar concentrations of sensitiser were added to a 2% red blood cell suspension and illuminated with red light. The release of haemoglobin was taken as the end-point of photo-haemolysis and was always preceded by the leakage of potassium (Fig. 8). No leakage of potassium or Hb was observed in the absence of light or sensitiser. PPC was the most efficient photosensitiser using this system, with the leakage of potassium detected within 1 min of illumination. TDOPc was slightly more efficient than PHP and *m*THPC, probably reflecting the increased extinction coefficient of the phthalocyanines in the red (Fig. 2). However, despite an increased absorption, TGly was the least effective photosensitiser, requiring longer illumination times for haemolysis to occur.

4. Discussion

Successful PDT requires that oxygen-dependent reactions occur. Upon absorption of light, photosensitising compounds can react with ground-state oxygen via type I or type II reaction pathways [29] to produce reactive oxygen species. These can then react with a variety of substrates such as proteins and lipids. The photo-oxidation of amino acids is a common method by which the photosensitising abilities of

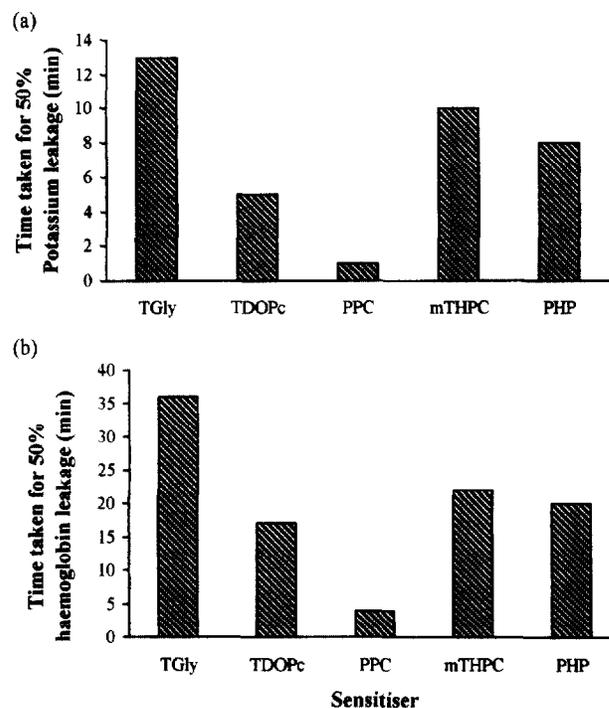


Fig. 7. The efficacy of each sensitiser (10 μ M) monitored by the time taken to cause 50% haemolysis of a 2% erythrocyte solution. Haemolysis was determined by (a) potassium ion release and (b) haemoglobin release.

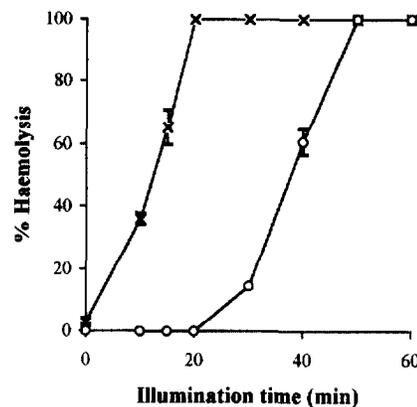


Fig. 8. The effect of illumination on the release of potassium ions (×) and haemoglobin (○) from a 2% erythrocyte suspension in the presence of TGly (10 μ M).

compounds are compared [23,30–32]. The efficacy of photosensitiser is affected by several parameters, such as the extinction coefficient at the treatment wavelength, the singlet oxygen yields, the availability of target molecules, hydrophobicity, charge and aggregation.

The influence of aggregation on photosensitising ability was studied by following the oxidation of Trp in a range of methanol solutions via the decrease in Trp fluorescence. In these experiments white light was used, therefore absorption of light would occur over the entire spectrum. Increasing the methanol concentration was accompanied by monomerisation (Fig. 2) and increased rates of Trp oxidation (Fig. 5). The bell-shaped curve observed with TGly and *m*THPC is similar to that observed with PPC and PHP [27] and to that

reported by others [30,32], with the ascending portion of the curve reflecting the increased sensitiser quantum yield and $^1\text{O}_2$ lifetime. At high concentrations of methanol these rate-enhancing factors are counteracted by a decrease in the Trp- $^1\text{O}_2$ reaction [30]. Maximal rates of reaction were observed in different methanol concentrations for each sensitiser (Table 2), reflecting the changes observed in aggregation state (Fig. 2). At the maximal rate, TGly was the most efficient, whilst *m*THPC and TDOPc were poor photosensitisers in this system.

Oxygen-consumption experiments supported the Trp oxidation experiments. In these experiments red rather than white light was used, therefore the Pcs would absorb more light than *m*THPC and PHP [11,14]. The efficacy of each sensitiser varied, but for a given photosensitiser the rates of Trp and His oxidation were very similar (Table 3). Fiedler et al. [31] have shown similar results with Photosan, a compound equivalent to PHP, but *m*THPC was shown to be more efficient at the oxidation of Trp than His. From the results shown in Table 3, it appears that the more hydrophilic sensitisers produce better photo-oxidation of these amino acids than the hydrophobic ones. The photo-oxidation of BSA was more efficient with all five photosensitisers, which probably reflects sensitiser monomerisation occurring in the presence of BSA (Fig. 6).

In biological fluids and cellular environments, photosensitisers can enter into additional interactions that alter their photophysical behaviour. Erythrocytes are a commonly used model for membrane damage, with disturbances in plasma membrane topology following photosensitisation followed by leakage of potassium, and eventually Hb [33–35]. This form of colloid osmotic lysis has been explained by the photo-oxidation of membrane proteins leading to crosslinking, and subsequent loss of cellular functions such as the transport of K^+ and Na^+ [33,34]. Using this system, the efficacy of photosensitisation was in the order PPC > TDOPC > PHP > *m*THPC > TGly (Fig. 7). This may reflect an increased affinity of the hydrophobic sensitisers for the lipophilic membrane of red blood cells. However, this cannot account for the rapid haemolysis observed with the hydrophilic PPC. It may be that the positive charge on this compound is responsible for its improved efficacy through an increased selectivity for critical targets [35].

In summary, PPC and TDOPc have improved photodynamic activity (with respect to red blood cell haemolysis) over the current clinical sensitisers, *m*THPC and PHP. Aggregation state, extinction coefficients, charge and hydrophobicity have been shown to be important determinants of activity; however, localisation at sensitive sites and singlet oxygen yields will also be influential. The phthalocyanines used in this study have similar singlet oxygen quantum yields to methylene blue (J. Schofield, personal communication), therefore this cannot explain the differences in efficacy between the three substituted phthalocyanines. Further studies on localisation using the RIF-1 cell line as a more complex cellular model are in progress.

5. Abbreviations

BSA	bovine serum albumin
Hb	haemoglobin
His	histidine
<i>m</i> THPC	5, 10, 15, 20-tetra(<i>m</i> -hydroxyphenyl)chlorin
PBS	phosphate buffered saline
Pc	phthalocyanine
PDT	photodynamic therapy
PEG	polyethylene glycol
PHP	polyhaematoporphyrin
PPC	pyridinium zinc (II) phthalocyanine
TDOPc	tetradioctylamine zinc (II) phthalocyanine
TGly	tetraglycine zinc (II) phthalocyanine
Trp	tryptophan

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