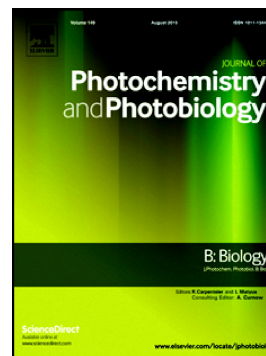


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Benzamide porphyrins with directly conjugated and distal pyridyl or pyridinium groups substituted to the porphyrin macrocycles: Study of the photosensitising abilities as inducers of apoptosis in cancer cells under photodynamic conditions

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Abstract: Amphiphilic porphyrin photosensitisers (PSS) having combinations of directly substituted pyridyl group(s) at the *meso*-position of a porphyrin macrocycle, and/or indirectly linked pyridyl groups as benzamide derivatives are reported. The compounds 5,10,15,20-tetrakis-(4-pyridylbenzamide)porphyrin (**A.2**), 5,10,15,20-tetra[N-(pyridine-4-yl)benzamidium] porphyrin (**A.3**), 5-mono-(4-pyridyl)-10,15,20-tris-(4-pyridylbenzamide)porphyrin (**B.2**) and 5-mono-(4-methylpyridinium)-10,15,20-tris-(4-pyridiniumbenzamide)porphyrin (**B.3**) were synthesised. The compounds were successfully characterised through UV-Vis, Emission, ¹HNMR, and ESI-HRMS techniques. To evaluate the effect of this combination of directly conjugated and non-conjugated pyridyl/cationic pyridinium groups on the porphyrin macrocycle, the efficacy of the synthesised compounds was compared to a known standard 5,10,15,20-tetrakis(1-methylpyridinium-4-yl)porphyrin (TMPyP). These compounds show better efficacy (IC₅₀'s ranging between 0.66±0.04 μM to 3.71±1.01 μM) against A549 (human epithelial adenocarcinoma lung cancer) cell line under *in vitro* photodynamic conditions in comparison to MDA-MB-231 (breast cancer) (IC₅₀'s ranging between 3.7±0.087 μM to 12.1±0.12 μM) and Pa-1 (ovarian cancer) (IC₅₀'s ranging between 17.9±0.01 μM to 42.45 ±0.02 μM) cell lines. It was found that **B.3**, having a pyridinium group attached to the *meso*-position of the macrocycle along with three distal cationic pyridinium groups, independent of the porphyrinic electron delocalisation cycle, showed better photocytotoxic efficacy (IC₅₀ = 0.66 ± 0.04 μM, A549 lung

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