A novel porphyrin-peptide derivative has been synthesized by a solid-phase peptide synthesis (SPPS) protocol, with the aim of defining a novel antimicrobial amphiphile

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The new molecule is constituted by a tetrapeptide chain of a repeated sequence of (D)Valine-(L)Lysine covalently linked by an amidic bond to the achiral 5- (4-carboxyphenyl)-10,15,20-(triphenyl)porphyrin, thus conferring chiral features to the macrocycle. The small peptide chain may have beneficial role as antimicrobial, due to the presence of two positively charged lysines able to disrupt the integrity of negatively charged bacterial cell membranes. Furthermore, the presence of the porphyrin ring may enhance the antimicrobial activity combining the peptide features to the possibility of irradiating the dye, with the generation of an excited triplet state that produces ROS, via an electron or energy transfer mechanism, destroying bacterial membranes (antimicrobial photodynamic therapy). The aggregation behaviour of the new molecule in aqueous environments has been also investigated, using PBS solutions in combination with increasing amounts of organic solvents (ethanol and DMSO), to understand the role of the solvent in driving the aggregation. Self-assemblies into curved sheets were revealed by TEM and confirmed by Cryo-TEM microscopy images. Strong chiral features of the aggregates were shown by Circular Dichroism spectroscopy and they can be related to the curvature of the sheets, as similarly observed in literature. Promising preliminary data of the antimicrobial activity suggested a synergic role between the porphyrin and the peptide chain since the tetrapeptide alone did not show cytotoxicity against bacteria. Based on these results, amphiphiles different for peptide sequences and porphyrin head will be synthesized to investigate and modulate the antimicrobial activity.