Compared to Purpurinimides, the Pyropheophorbide Containing an Iodobenzyl Group Showed Enhanced PDT Efficacy and Tumor Imaging (^{124}I-PET)

Suresh K. Pandey, Munawwar Sajjad, Yihui Chen, Anupam Pandey, Joseph R. Misser, Carrie Batt, Rutao Yao, Hani A. Nabi, Allan R. Oseroff, and Ravindra K. Pandey

Abstract

Two positional isomers of purpurinimide, 3-[1′-(3-iodobenzyloxyethyl)] purpurin-18-*N*-hexylimide methyl ester **4**, in which the iodobenzyl group is present at the top half of the molecule (position-3), and a 3-(1′-hexyloxyethy)purpurin-18-*N*-(3-iodo-benzylimide)] methyl ester **5**, where the iodobenzyl group is introduced at the bottom half (N-substitued cyclicimide) of the molecule, were derived from chlorophyll-*a*. The tumor uptake and phototherapeutic abilities of these isomers were compared with the pyropheophorbide analogue **1** (lead compound). These compounds were then converted into the corresponding ^{124}I-labeled PET imaging agents with specific activity >1 Ci/μmol. Among the positional isomers **4** and **5**, purpurinimide **5** showed enhanced imaging and therapeutic potential. However, the lead compound **1** derived from pyropheophorbide-*a* exhibited the best PET imaging and PDT efficacy. For investigating the overall lipophilicity of the molecule, the 3-*O*-hexyl ether group presnt at position-3 of purpurinimide **5** was replaced with a methyl ether substituent, and the resulting product **10** showed improved tumor uptake, but due to its significantly higher uptake in the liver, spleen, and other organs, a poor tumor contrast in whole-body tumor imaging was observed.