

Combining Devices and Drugs by Synthetic Natural Product Hybrids

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INTRODUCTION: Natural products contain the evolutionary wisdom of ages and only synthetic organic chemistry can unlock their full potential. Hybridization of natural products by combining fragments with different bioactivity presents an appealing strategy to modify and to leverage given properties.¹ Traditional approaches to natural product hybridization involve the combination of two natural pharmacophores by a covalent linker without impacting the biological activity of each fragment.¹ Moreover, higher order hybrids can be obtained by linking several components together, either covalently or by self-assembly. In this communication, we demonstrate the preparation of quaternary natural product hybrids.

METHODS: Recently, a biomimetic linker for ultramild surface functionalization was introduced, relying on powerful catechol metal oxide interactions.² This linker has been used to render surfaces resistant to fouling,² a serious problem in many areas ranging from water technology to medicine.³

RESULTS: We have prepared through organic chemistry a series of complex ternary hybrids linking the anachelin chromophore as biomimetic linker via a PEG spacer to various biologically active natural products. In addition, these compounds were hybridized to surfaces thus generating unique quaternary hybrids (Fig. 1).

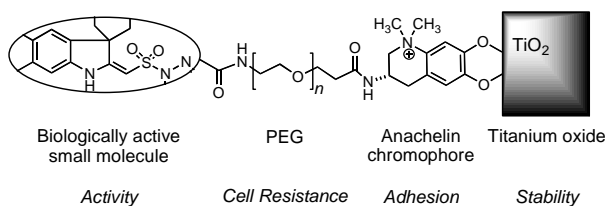


Fig. 1: Quaternary natural product hybrids linking a surface such as a metal oxide (stability) via the linker (adhesion) and a PEG spacer (providing cell resistance) to a natural product with powerful biological activity.

DISCUSSION & CONCLUSIONS: A novel approach for the generation of bioactive surfaces is presented. The utilization of natural product hybrids is very promising, as distinct features of each component can be hybridized and their properties leveraged. The quaternary hybrids are thus merging properties such as stability, surface adhesion, protein/cell resistance, and pronounced biological activity for the generation of antimicrobial surfaces or antifungal surfaces. Therefore, devices and drugs can be combined through synthetic natural product hybrids.

REFERENCES: ¹ K. Gademann (2006) *Chimia* **60**:841-845. ([fulltext](#)).

² S. Zuercher, D. Waeckerlin, Y. Bethuel, B. Malisova, M. Textor, S. Tosatti, K. Gademann (2006) *J. Am. Chem. Soc.* **128**:1064-1065. ([fulltext](#)).

³ K. Gademann (2007) *Chimia* **61**:373-377. ([fulltext](#)).