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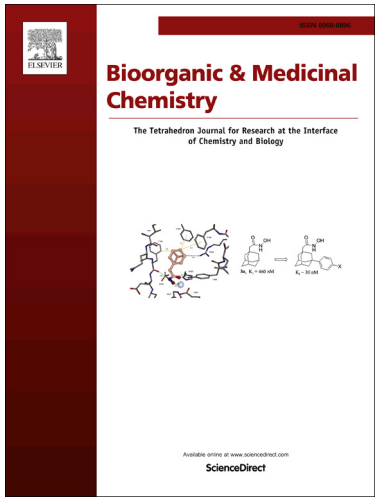

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Guanine-based amphiphiles: synthesis, ion transport properties and biological activity

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Abstract. Novel amphiphilic guanine derivatives, here named **Gua1** and **Gua2**, have been prepared through few, simple and efficient synthetic steps. In ion transport experiments through phospholipid bilayers, carried out to evaluate their ability to mediate H^+ transport, **Gua2** showed high activity. When this compound was investigated for ion-selective transport activities, no major differences were observed in the behaviour with cations while, in the case of anions, selective activity was observed in the series $I^->Br^->Cl^->F^-$. The bioactivity of these guanine analogues has been evaluated on a panel of human tumour and non-tumour cell lines in preliminary *in vitro* cytotoxicity assays, showing a relevant antiproliferative profile for **Gua2**.

Keywords: guanine derivatives; amphiphiles; synthetic ionophores; *in vitro* bioactivity tests.

Introduction

Among the canonical nucleobases, guanine plays a special role, having an extraordinary ability to produce multiple hydrogen bonds and thus generate not only Watson-Crick interactions but also a variety of non-Watson-Crick specific recognition schemes [1]. Thus, either in the form of single base or nucleoside, or incorporated in guanine-rich oligonucleotides, guanine derivatives may result into higher order self-assembling arrangements, such as the G-quadruplex structures, which are complex three-dimensional architectures consisting of stacked G-tetrads stabilized by Na^+ or K^+ cations [2-4].

As a general remark, the biological activity of guanines and guanosines is not only related to their incorporation into specific DNA and/or RNA sequences, but can be found also in single nucleosides/nucleotides and/or nucleoside analogues. The stringent need for effective antiviral drugs has been the main trigger for the research in the field of nucleoside analogues in the last three decades. These efforts have produced a plethora of new, diverse compounds, many of which endowed with relevant bioactivity [5,6]. Well known examples of antiviral modified guanosines are acyclovir [7], ganciclovir [8] and entecavir [9], which are currently adopted in clinic against HSV,