Accepted Manuscript

Alkyl-substituted phenyl-amino derivatives of 7-nitrobenz-2-oxa-1,3-diazole as uncouplers of oxidative phosphorylation and antibacterial agents: involvement of membrane proteins in the uncoupling action

Yuri N. Antonenko, Stepan S. Denisov, Ljudmila S. Khailova, Pavel A. Nazarov, Tatyana Rokitskaya, Vadim N. Tashlitsky, Alexander M. Firsov, Galina A. Korshunova, Elena A. Kotova

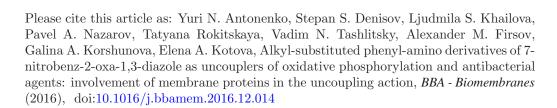
PII: S0005-2736(16)30407-2

DOI: doi:10.1016/j.bbamem.2016.12.014

Reference: BBAMEM 82377

To appear in: BBA - Biomembranes

Received date: 22 August 2016 Revised date: 15 December 2016 Accepted date: 19 December 2016



This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Alkyl-substituted phenyl-amino derivatives of 7-nitrobenz-2-oxa-1,3-diazole as uncouplers of oxidative phosphorylation and antibacterial agents: involvement of membrane proteins in the uncoupling action

Yuri N. Antonenko^{1*}, Stepan S. Denisov^{1,2}, Ljudmila S. Khailova¹, Pavel A. Nazarov¹, Tatyana Rokitskaya¹, Vadim N. Tashlitsky², Alexander M. Firsov¹, Galina A. Korshunova¹, Elena A. Kotova^{1*}

¹Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, and ²Faculty of Chemistry, Lomonosov Moscow State University, Leninskie Gory 1, Moscow 119991, Russia

*Address correspondence to: Yuri Antonenko, Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, Moscow 119991, Russia. Fax:+(7-495)-939-31-81, E-mail: antonen@genebee.msu.ru

Elena A. Kotova, Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, Moscow 119991, Russia; Fax:+(7-495)-939-31-81, e-mail: kotova@genebee.msu.ru

ABSTRACT

In search for new effective uncouplers of oxidative phosphorylation, we studied 4-aryl amino derivatives of a fluorescent group 7-nitrobenz-2-oxa-1,3-diazol (NBD). In our recent work (Denisov et al., Bioelectrochemistry, 2014), NBD-conjugated alkyl amines (NBD-C_n) were shown to exhibit uncoupling activity. It was concluded that despite a pK_a value being about 10, the expected hindering of the uncoupling activity could be overcome by insertion of an alkyl chain. There is evidence in the literature that the introduction of an aryl substituent in the 4-amino NBD group shifts the pK_a to neutral values. Here we report the data on the properties of a number of 4-arylamino derivatives of NBD, namely alkylphenyl-amino-NBD (C_n-phenyl-NBD) with varying alkyl chain C_n. By measuring the electrical current across planar bilayer lipid membrane, the protonophoric activity of C_n-phenyl-NBD at neutral pH grew monotonously from C₁- to C₆-phenyl-NBD. All of these compounds increased the respiration rate and reduced the membrane potential of isolated rat liver mitochondria. Importantly, the uncoupling action of C₆-and C₄-phenyl-NBD was partially reversed by glutamate, diethyl pyrocarbonate (DEPC), 6-ketocholestanol and carboxyatractyloside, thus pointing to the involvement of membrane proteins in the uncoupling activity of C_n-phenyl-NBD in mitochondria. The pronounced

Download English Version:

https://daneshyari.com/en/article/5507349

Download Persian Version:

https://daneshyari.com/article/5507349

<u>Daneshyari.com</u>