

## Accepted Manuscript

Title: Pharmacokinetic profile of promising acetylcholinesterase reactivators K027 and K203 in experimental pigs

Author: Jana Zdarova Karasova Jaroslav Kvetina Ilja Tacheci  
Vera Radochova Kamil Musilek Kamil Kuca Jan Bures



PII: S0378-4274(17)30119-4  
DOI: <http://dx.doi.org/doi:10.1016/j.toxlet.2017.03.017>  
Reference: TOXLET 9728

To appear in: *Toxicology Letters*

Received date: 2-2-2017  
Revised date: 13-3-2017  
Accepted date: 15-3-2017

Please cite this article as: Karasova, J.Z., Kvetina, J., Tacheci, I., Radochova, V., Musilek, K., Kuca, K., Bures, J., **Pharmacokinetic profile of promising acetylcholinesterase reactivators K027 and K203 in experimental pigs**, *Toxicology Letters* (2017), <http://dx.doi.org/10.1016/j.toxlet.2017.03.017>

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.

## Pharmacokinetic profile of promising acetylcholinesterase reactivators K027 and K203 in experimental pigs

Jana Zdarova Karasova,<sup>1,2</sup> Jaroslav Kvetina,<sup>3</sup> Ilja Tacheci,<sup>3</sup> Vera Radochova,<sup>4</sup> Kamil Musilek,<sup>1,2</sup> Kamil Kuca<sup>2</sup> and Jan Bures<sup>3</sup>

<sup>1</sup> Department of Toxicology and Military Pharmacy, Faculty of Military Health Sciences, Hradec Kralove, Czech Republic

<sup>2</sup> Biomedical Research Center, University Hospital, Hradec Kralove, Czech Republic

<sup>3</sup> 2nd Department of Medicine - Gastroenterology, Charles University Faculty of Medicine and University Hospital, Hradec Kralove

<sup>4</sup> Department of Military Surgery, Faculty of Military Health Sciences, Hradec Kralove, Czech Republic

Corresponding author: Dr. Jana Zdarova Karasova, PhD. Department of Toxicology and Military Pharmacy, Faculty of Military Health Sciences Trebesska 1575, 500 01 Hradec Kralove Czech Republic Tel: +420-973-253-116 Email: [zdarova.jana@gmail.com](mailto:zdarova.jana@gmail.com)

### Abstract

Standard treatment of organophosphorus compounds (OPs) poisoning includes administration of an anti-muscarinic (atropine), anticonvulsive (diazepam) and acetylcholinesterase reactivator (oxime). From a wide group of newly synthesized oximes, oxime K027 and oxime K203 seem to be perspective compounds in some specific OPs intoxication. The available *in vitro* and *in vivo* preclinical data indicate that both oximes may be considered for potential human use. The main aim of this study was to establish plasmatic concentration curves of both oximes after intramuscular (i.m.) and intragastric (i.g.) application with subsequent pharmacokinetic analysis and study distribution after (i.m.) application on a non-rodent animal model (experimental pigs; 1500 mg/animal).

According to the results, both oximes had similar  $C_{\max}$  (K027:  $106 \pm 19 \mu\text{g/mL}$  and K203:  $111 \pm 8 \mu\text{g/mL}$ ) in  $T_{\max}$   $19 \pm 5 \text{ min}$ , respectively in  $22 \pm 3 \text{ min}$ . Bioavailability of oxime K027 calculated as  $AUC_{\text{total}}$  ( $8389 \pm 1024 \text{ min} \cdot \mu\text{g/mL}$ ) was halved compared to oxime K203 (16938

Download English Version:

<https://daneshyari.com/en/article/5562102>

Download Persian Version:

<https://daneshyari.com/article/5562102>

[Daneshyari.com](https://daneshyari.com)