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Stability monitoring of some acetylcholinesterase reactivating drugs

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Background

Widespread use of organophosphorous compounds (OPs) in agriculture and as nerve agents as well as a lack of clinically effective antidotes initiated the synthesis of new pyridinium bis-aldoximes (K-compounds) with high potency in reactivating acetylcholinesterase irreversibly inhibited by OPs [1,2]. We aimed to optimize an HPLC method sensitive enough to determine K-compounds from different biological matrices (blood, brain and cerebrospinal fluid) [3,4].

Methods

Samples of biological origin needed proper clean-up. An RP-HPLC method using either UV and amperometric detector was used following separation on a Zorbax Rx-C18 octadecyl silica column with a mobile phase of phosphate buffer with 20% acetonitrile (pH 3.7). 1-Octane sulphonic acid sodium salt (OSA) was used as ion-pairing agent. Calculation of theoretical plate number, asymmetry of peaks, limit of quantitation (LOQ), lower limit of detection (LLOD) and determination of pH, temperature and OSA concentration dependence was done.

Results

Elution characteristics of bis-pyridinium mono-aldoximes were depending on the OSA concentration, however, to a lesser extent than the bis-pyridinium bis-aldoximes. A double bond in the alkyl chain decreased the dependence from the ion-pairing agent concentration only to a minor extent. When the samples were kept at a pH under 1.5 a peak of degradation product was generated. The time course of degradation in an acidic milieu was calculated.

Conclusions

Appropriate clean-up, optimal concentration of the ion-pairing agent and a well-selected mode of detection are the key factors for optimal determinations. We point out decomposition of pyridinium aldoximes at acidic pH.

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