## Abstract

Co-administration of oxime reactivators of AChE together with atropine and diazepam is the basic strategy for the pharmacological treatment of organophosphate (OP) poisoning. The aim is to develop such oxime, that would be effective against a wide range of OPs and simultaneously, that would penetrate the central nervous system.

Bispyridinium oximes are among the structures with the most efficient acetylcholinesterase reactivation. However, they are charged molecules that poorly cross the blood-brain barrier. Researchers try to modify these molecules to be more lipophilic thus, enhancing their central effect. One of the possible approaches is to substitute the basic structure of the reactivator with suitable functional groups. K869 is an asymmetric bispyridinium oxime whose pyridinium ring is substituted by two chlorine atoms.

An HPLC-UV method was developed and optimized for the determination of oxime K869 in plasma and kidneys. Since oxime K869 is a permanently charged molecule, ion- pair chromatography was applied, in which the molecule becomes uncharged with the addition of an ion-pairing agent (1 mM octane sulfonic acid) to the aqueous components of the mobile phase (citrate-phosphate buffer). It was then separated in a reverse chromatographic mode in isocratic elution mode where acetonitrile was an organic phase (14 %). An SPE method using Weak-Cation Exchange columns was developed for sample adjustment. A mixture of acetonitrile, formic acid, and water in a ratio of 9: 0.5: 0.5 (v/v/v) were used as eluent. Plasma concentrations peaked ~ 40 μg/mL between 15 and 20 minutes after administration. The highest renal concentration was measured ~ 20 μg/mL in samples collected 30 and 60 minutes after administration.